WORKING MEMORY AND SENTENCE COMPREHENSION IN PARKINSON'S DISEASE PATIENTS ON AND OFF MEDICATION

By

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To investigate the role of the basal ganglia in working memory and sentence comprehension, 14 Parkinson's disease (PD) patients were administered experimental measures of semantic and phonological working memory, and a measure of sentence comprehension, with dopamine at peak levels and after a period of dopamine withdrawal. An age- and education-matched control group (N=14) received the same measures. Results indicated significant changes in motor functioning related to dopamine in PD patients, with no changes in cognitive measures. The control group showed superior performance on sentence comprehension and one measure of working memory compared to the PD patients. Results suggest that basal ganglia dysfunction, as

measured through dopamine manipulation, is not the sole factor contributing to cognitive deficits seen in PD.

INTRODUCTION

The goal of the present study is to explore the effect of Parkinson's disease (PD) on working memory. This will allow for examination of the role that subcortical structures may play in working memory. The rationale for exploring possible working memory deficits in patients with PD lies in the anatomic connections between the subcortical structures principally affected in PD and frontal cortical areas thought to be important to working memory. Degeneration of subcortical structures may be expected to have an impact on cortical areas due to a breakdown of cortico-striato-pallido-thalamo-cortical circuits (Alexander et al., 1986) ultimately resulting in an alteration of frontal lobe functioning. Due to the fact that the dopamine is both the primary neurotransmitter in the basal ganglia and the primary neurotransmitter affected in PD, manipulation of dopamine allows for examination of the impact that altered functioning of the basal ganglia may have on cortical structures. One way to measure this impact on the frontal lobes is by measuring working memory, a cognitive process thought to involve the frontal lobes (Fuster, 1984; Goldman-Rakic, 1990). The expectation of the current

study was that decreases in dopamine levels would result in decreases in working memory tested by several measures. The following review will further develop the theoretical rationale for this study by examining general subcortical anatomy, the pathophysiology of PD, research implicating the frontal lobes in different aspects of working memory, and research suggesting deficits in frontal lobe functioning in patients with PD.

REVIEW OF LITERATURE

Anatomy and Function of Basal Ganglia-Thalamocortical Circuits

In order to understand the potential effect of PD on working memory, it is necessary to consider the relevant anatomy of the basal ganglia and to consider how these structures may affect cortical function. The basal ganglia have been implicated in a variety of behavioral dimensions, including motor, cognitive, and emotional functions. Alexander et al. (1986) have postulated several parallel cortico-striato-pallido-thalamo-cortical circuits, which are functionally and anatomically segregated, but have similar anatomic organization. In an extensive review of these circuits, Alexander et al. (1990) described the similarities among "motor," "oculomotor," "limbic," "dorsolateral prefrontal," and "lateral orbitofrontal" circuits. They reported that specific cortical areas have excitatory glutamatergic projections to specific portions of the striatum, including the caudate nucleus, putamen, and the ventral striatum. These are described as the inputs to the circuits. The output of striatal spiny neurons (the most common striatal neuron) is characterized by a distinct pattern of long periods of silence with brief periods of

activity lasting tenths of seconds to seconds (Wilson, 1995). Evidence suggests that the cortical input to striatal neurons is phasic and correlated with the striatal bursts of activity. The internal segment of the globus pallidus (GPi), substantia nigra pars reticulata (SNr), and the ventral pallidum, the targets of striatal output, project to the thalamus. They have a high rate of spontaneous discharge. Both the striato-pallidal and the pallido-thalamic connections are inhibitory.

Within each circuit Alexander et al. (1990) describe direct and indirect pathways. The "direct" pathway emanates from striatal neurons containing gamma aminobutyric acid (GABA) and substance P, and projects to GPi and SNr. The net result of activation of these striatal neurons is a disinhibition of the thalamus. An "indirect" pathway from striatal neurons containing GABA and enkephalins to GPi and SNr passes through the external segment of the globus pallidus (GPe). The pathway continues from GPe to the subthalamic nucleus (STN) with a GABAergic projection and connects the STN to GPi and SNr with an excitatory projection, that is probably glutamatergic. The high discharge rate of GPe neurons thereby has a tonic inhibitory influence on the STN; therefore, excitation of the GABA-enkephalin striatal neurons suppresses activity of GPe neurons, thus disinhibiting STN and increasing the excitation of GPi and SNr. The net result of an increase in activity of GPi and

SNr is increased inhibition of the thalamus. Alexander et al. (1990) described the "indirect" and "direct" pathways as having opposing effects on the GPi and SNr, and, therefore, having opposing effects on the thalamic targets of these structures. However, they note that there is a paucity of information concerning the nature of the interaction of these two pathways within individual basal ganglia output neurons.

The mechanism through which cortical control is affected has been most extensively explored in movement. Alexander et al. (1990) indicate that movement related neurons in the GPi and SNr show either phasic increases or phasic decreases in their rates of discharge during specific limb or orofacial movements. They suggest that phasic decreases in GPi and SNr output influence movement by disinhibiting the ventrolateral thalamus, thereby facilitating cortically initiated movements, while phasic increases in GPi and SNr output perform the opposite role. The authors point to conditions of hypokinesia or akinesia that are associated with tonic increases of GPi and STN firing rates as evidence of this hypothesis. Conversely, lesions of the STN leading to involuntary hyperkinesia, are associated with tonic reductions in firing rates of GPi neurons (Mitchell, Jackson, Sambrook, & Crossman, 1989).

Dopamine plays an integral role in basal ganglia functions. In a comprehensive review, Wichmann and DeLong

(1993) describe the complex role dopamine appears to play in the control of movement. The general activity of the basal ganglia-thalamocortical connections is modulated by dopaminergic projections from the substantia nigra pars compacta. They describe three dopaminergic pathways involved in the basal ganglia-thalamocortical circuits: a nigrostriatal pathway, a nigropallidal pathway with projections mainly to GPi, and a possible small projection to the STN. Dopamine appears to have contrasting effects on the "direct" and "indirect" pathways of the basal ganglia. Dopamine appears to have a net excitatory input on the "direct" pathway between the striatum and the GPi and SNr, while it has a net inhibitory influence on the "indirect" pathway connecting the striatum to the GPe. This dual role of dopamine is believed to result in reinforcement of cortically initiated activation of basal ganglia-thalamocortical circuitry by focusing the input to the thalamus through a strengthening of activity in the "direct" basal ganglia pathways with a concurrent reduction of activity in the "indirect" pathways.

The basal ganglia-thalamocortical "motor circuit" has been implicated in the pathophysiology of motor impairments resulting from PD. Wichmann and DeLong (1993) described the primary pathophysiology of PD as consisting of the destruction of dopaminergic neurons projecting to the basal ganglia. The authors report that electrophysiological and metabolic studies in non-humans

with MPTP induced parkinsonism have revealed significant changes in the "motor" circuit in general, and specifically in the "indirect" pathway. These changes are consistent with the model presented above. The loss of striatal dopamine leads to over inhibition of GPe, which results in disinhibition of the STN. Increased STN activity leads to increased excitation of GPi, thereby increasing thalamic inhibition. At the same time, the loss of dopaminergic input to the striatum also leads to a decrease in activity in the "direct" inhibitory pathway from the striatum to GPi and SNr, which leads to further thalamic inhibition.

The "dorsolateral prefrontal" circuit is the basal ganglia-thalamic circuit most associated with working memory (Goldman-Rakic, 1990). According to Mega and Cummings (1994), the dorsolateral prefrontal cortex (DLPC) provides a major portion of the cortical input to the dorsolateral prefrontal circuit. The DLPC (Brodmann's areas (BA) 9, 10; Walker's area 46) has been defined as the area in and around the principal sulcus on the dorsal prefrontal convexity in monkeys. The dorsolateral head of the caudate receives projections from the DLPC. In addition, BA 7 of the posterior parietal cortex, which has reciprocal connections with the DLPC, also projects to the dorsolateral head of the caudate; however, parietal and frontal projections to the caudate head have been shown to be generally segregated rather than overlapping.

Percheron, Yelnik, and François (1984) initially proposed that these projections are subsequently integrated at the level of the globus pallidus, although this view was later revised to suggest the pathways remain segregated within the globus pallidus (Percheron & Fillon, 1991). However, this leaves unanswered where the loops overlap prior to projecting back to the frontal cortex, as some overlap seems likely. In the direct pathway, the caudate nucleus projects to the lateral region of the dorsomedial GPi and to the rostrolateral SNr. In the indirect pathway, the caudate projects to the dorsal GPe, which then sends projections to the lateral STN. The STN has projections to the GPi and SNr. The parvocellular portions of the ventral anterior and dorsomedial thalamus then receive input from these structures. The circuit is completed by projections from the dorsomedial and ventral anterior thalamus to the dorsolateral prefrontal lobe.

The existence of these circuits has led to the development of a fronto-striatal theory of cognitive function and dysfunction. The "dorsolateral prefrontal," "orbitofrontal," and "cingulate" loops are the circuits most associated with cognition. Several authors have incorporated the breakdown of the "complex" (e.g. non-motor) basal ganglia-thalamocortical connections in an effort to explain the "frontal-like" deficits that may appear in subcortical diseases, such as PD (Bondi, Kaszniak, Bayles, & Vance, 1993; Cummings & Benson, 1990;

Owen et al., 1992; Taylor et al., 1986). Cummings and Benson (1990) proposed that diseases that alter motor function through damage to the basal ganglia-thalamocortical circuits may simultaneously affect cognition through damage to the parallel circuits mediating cognition. Similarly, Taylor et al. (1986) proposed that the dopamine deficiency that occurs in PD may affect cognition due to caudate dysfunction. They suggested that the cognitive consequences could best be predicted by examining the cortical destination of basal ganglia-thalamocortical pathways, since the cortical input into the system is relatively widespread compared to the outflow from the thalamus. The authors noted that functions associated with the prefrontal region should be most detrimentally affected according to this theory, as a large portion of subcortical output terminates in prefrontal cortex.

This hypothesis that damage to the basal ganglia-thalamocortical loops affects prefrontal cortical areas has been supported by several studies examining the behavioral and physiological effects of basal ganglia lesions on cortical circuits (Divac et al., 1967; Isseroff et al., 1982; Kuhl et al. 1982). In an early study, Isseroff et al. (1967) found that lesions of the head of the caudate nucleus (in areas that receive input from DLPC) resulted in impairments on a spatial delayed alternation task similar to those results from direct

damage to the DLPC. Selective lesions of the caudate in areas that receive input from lateral orbitofrontal cortex were found to selectively impair primates in an object discrimination reversal task, a task thought to be sensitive to orbitofrontal cortical damage. Goldman and Rosvold (1972) found similar results following selective caudate lesions in infant and juvenile primates. Isseroff et al. (1982) lesioned the mediodorsal nucleus of the thalamus (MD), which has reciprocal connections with prefrontal cortex and is a component of the DLPC-basal ganglia circuit, and found that primates were impaired on both spatially delayed alternation and delayed response tasks. In addition, the behavioral impairment was correlated with the extent of destruction in posterior MD. Taken together, these studies raise the possibility of a role for the basal ganglia in cognition in primates. Unfortunately, both caudate and dorsomedial thalamic lesions directly damage DLPC afferents or efferents. Thus the resultant impairment in DLPC function could have been due to such direct damage rather than basal ganglia circuit dysfunction.

With regard to basal ganglia lesions in humans, Bhatia and Marsden (1994) performed a metanalysis of behavior and movement disorders in 240 patients with lesions involving the caudate nucleus, putamen, and globus pallidus. The authors categorized the lesions on the basis of location and size. Generally, they reported that

deficits involving the motor system were related to lesions of the lentiform nuclei, while behavioral deficits were associated with caudate lesions. The primary behavioral disturbance resulting from lesions of the caudate was abulia. The authors attributed the abulia symptoms to a breakdown of the basal ganglia-thalamocortical loops affecting the prefrontal cortex. They described the abulia as reflecting signs of a classic frontal syndrome. Bhatia and Marsden conjectured that cognitive impairments also may have been present in many cases. However, the appropriate neuropsychological testing was not performed in most of the cases they examined, indicating the role of the striatum in cognition is still open to speculation. Furthermore, in most of the cases reviewed, caudate damage was either associated with deep frontal white matter lesions capable of disconnecting the frontal lobes (particularly from the thalamus), or with large vessel thrombo-embolic occlusions that produced cortical ischemic damage often not apparent on imaging studies (Nadeau & Crosson, 1997). One method for gaining understanding about the function of the striatum is to examine deficits following striatal dysfunction, as occurs in PD. In order to appreciate the range of deficits possible in PD, it will be necessary to describe the pathophysiology of PD.

Pathophysiology of Parkinson's Disease

The symptomatology of idiopathic PD includes resting tremor, muscular rigidity, bradykinesia, gait disturbances and loss of postural reflexes. Characteristically, PD involves focal depletion of melanin-containing cell bodies in the central and caudal parts of substantia nigra pars compacta, neuronal loss in the locus ceruleus, and variable involvement of the nucleus basalis of Meynert and other subcortical structures (Jellinger, 1987). Other authors have noted significant cortical and subcortical atrophy, as well as gliosis in PD patients (de la Monte et al., 1989). Gibb (1993) reported that 60 to 80% of melanized pars compacta neurons may be lost, with ventral tier neurons showing a greater vulnerability than dorsal tier neurons. The ventral pars compacta projects to the dorsal caudate, while the dorsal pars compacta projects to the ventral caudate, resulting in a greater disease effect on the dorsal striatum (Gibb & Lees, 1991).

The degeneration of the nigrostriatal system leads to widespread effects in the dopaminergic system and is associated with changes in other neurotransmitter systems. With regard to the dopaminergic systems, degeneration affects the nigrostriatal, mesocortical, mesolimbic, and hypothalamic dopaminergic systems (Javoy-Agid & Agid, 1980; Jellinger, 1987). The greatest degenerative impact appears to be in the putamen, where virtually complete DA depletion has been documented in post-mortem studies, with

the most dramatic depletion taking place in the caudal putamen where less than 1% of the DA may remain. The dorsal rostral portion of the caudate nucleus has also been shown to have up to 96% loss of DA in PD (Kish et al., 1988; Lloyd et al., 1975). The primary cortical input to this area comes from the DLPC (Mega & Cummings, 1994), suggesting that depletion in this area may impact the output from the DLPC.

Decreases in acetylcholine in the cerebral cortex and hippocampus have been observed in PD and several authors have proposed that these changes may be related to the occurrence of dementia in PD (Agid et al., 1987; Dubois et al., 1983; Ruberg et al. 1982). On the basis of the forgoing description of structures affected in PD, it would appear to be reasonable to expect cognitive deficits. However, due to concomitant cortical degeneration also apparent in PD, it is important to try to distinguish cortical from basal ganglia effects. One domain where cognitive deficits may be measurable is working memory, and a method to distinguish cortical from basal ganglia effects is through manipulation of DA levels.

Anatomical and Functional Aspects of Working Memory

In examining the relationship between working memory and PD, it is important to consider anatomical aspects of working memory. Before describing anatomical features of working memory, the term must first be defined. Since the

term "working memory" was first introduced (Baddeley & Hitch, 1974), it has been used to refer to several related, but differing concepts. Baddeley and Hitch (1994) described three of these. The first concept they described refers to computational models of memory and involves the storage of particular computational productions. The second concept they described focuses on working memory as being a system that combines both storage and processing of incoming information. The third interpretation the authors described was their own original conceptualization that involved segregation of working memory into subcomponents, consisting of the phonological loop, the visuospatial sketchpad, and a central executive. This last definition is the most narrow and has traditionally been associated with anatomic and neuropsychological research into working memory in humans. With some exceptions (e.g. Just & Carpenter, 1992; Martin, 1994), Baddeley and Hitch's concept of working memory has provided the impetus for much research into the area of working memory and will be discussed in further detail due to its heuristic value and its widespread use in relevant literature, although there are several areas where the model is less than complete.

Baddeley and Hitch (1994) described the phonological loop as involving a phonological store within which memory traces fade after about 2 s if they are not revived by an articulatory process which refreshes the memory trace

through subvocal rehearsal. Although Baddeley and Hitch did not discuss anatomical implications of their model, the phonological store could be interpreted as residing in the linked acoustic and articulatory components of the phonological processor. As evidence of the phonological loop, the authors cited 4 phenomena. The first was the phonological similarity effect, in which immediate serial recall is impaired when items are similar in sound (Conrad & Hull, 1964). The second was the irrelevant speech effect, which refers to the fact that spoken material a subject has been instructed to ignore may impair verbal serial recall of numbers or letters, without regard to lexical or semantic characteristics of the distracting material (Colle & Welsh, 1976: Salamé & Baddeley, 1982). The third was the word length effect, where immediate memory span declines with the spoken length of the items to be remembered (Baddeley et al., 1975). The final phenomenon Baddeley and colleagues cited was articulatory suppression, where a distractor task that prevents subvocal rehearsal, results in impaired performance and a loss of the word length effect (Baddeley et al., 1984).

The visuospatial sketchpad and the central executive components of their model are less well developed (Baddeley & Hitch, 1994). The sketchpad is a specialized mechanism engaged in processing and storage of visual and/or spatial material. The concept was developed to account for the fact that visuospatial and verbal working

memory appear to involve separate resources. Evidence for the sketchpad mainly arises from dual task paradigms, in which selective spatial interference impairs memory on spatial tasks (Baddeley et al., 1975). The central executive is the least well defined area of Baddeley and Hitch's model. It is described as being responsible for coordinating attentional resources, and coordinating incoming information from the slave systems (Baddeley, 1986; 1992; Baddeley and Hitch, 1994). The central executive has been compared to the supervisory attentional system (SAS) proposed by Norman and Shallice (1980). Baddeley (1986) interpreted the SAS as being used to consciously direct attention to a particular stimulus. Baddeley acknowledged that his model of working memory is not complete, particularly with respect to the central executive and suggested that there may be other slave systems in addition to the phonological loop and the visuospatial sketchpad.

One area Baddeley and Hitch (1994) did not discuss is the role that semantics may play in verbal working memory. Numerous studies have suggested that material stored as phonologic working memory may be additionally represented as lexical-semantic working memory, depending on the semantic context of the material to be remembered (Brooks & Watkins, 1990; Crowder, 1978; Potter, 1993; Salamé & Baddeley, 1982; Schweickert, 1993;). In a specific example, Hulme et al. (1991) found that memory span for

nonwords was consistently lower than memory span for real words, which carry semantic content. Similarly, the span for Italian words was lower than the span for English words in English speaking participants. However, learning the English translations for the Italian words increased the participants' memory span. This suggests that the "pure" form of the phonological loop may be used exclusively in special circumstances, while in other cases there may be different systems used in conjunction with, or separately from, the phonological loop.

Based on these studies, it appears that even a relatively discrete task, such as within span word list learning, draws on several components of memory, including phonological and lexical-semantic elements. This has led to the development of models of language comprehension that postulate forms of working memory that include lexical-semantic elements, in contrast to a reliance only on phonologic elements implied in Baddeley's (1986) working memory model. Studies involving patients with specific memory deficits have also provided evidence for lexical-semantic contributions to working memory. Baddeley, Papagno, and Vallar (1988) reported a patient, P.V., who showed normal ability to learn pairs of meaningful words; however, she was severely impaired in her ability to learn associations between a familiar word and an unfamiliar word from a foreign language using auditory presentation. The authors suggested that her

phonological short-term store was not functional, and she was taking advantage of semantic elements in the words for memorization, providing further evidence for a semantic contribution to short-term memory. Other studies have found similar results in patients with selective deficits in the phonological loop (Belleville, Peretz, & Arguin, 1992; Martin & Romani, 1994; Trojano, Stanzione, & Grossi, 1992).

The Baddeley and Hitch (1974) model of working memory has largely been used to explore the human anatomy of working memory. Petrides, Alivisatos, Meyer, and Evans (1993) measured regional cerebral blood flow (rCBF) during a verbal working memory task. In the control task, the subjects counted aloud from 1 to 10. In a self-ordered condition, subjects randomly ordered numbers from 1 to 10 without repetition. In the externally ordered condition, a random sequence of the numbers from 1 to 10 was read to the subjects, with one number omitted. The subjects were to respond with the number that had been omitted. Using a subtraction method to measure the different levels of activation between the different conditions, both experimental tasks showed bilateral activation of mid-dorsolateral frontal cortex (BA 9 and 46) compared to the control task. There were no significant differences between the experimental conditions in those areas. There was also an increase in rCBF in frontopolar cortex (BA 10) in the external task. Based on these results, the authors

suggested that the DLPC is involved in working memory regardless of whether the task is internally or externally oriented. It is important to note that these tasks did not involve semantic factors and would therefore be most relevant when conceptualized in terms of Baddeley and Hitch's model of working memory with emphasis on the phonological loop.

The animal literature has also provided important information concerning the nature and anatomy of working memory. Goldman-Rakic (1990) proposed that nonhuman primates engage in a form of working memory when they perform delayed-response tasks. These tasks require updating and keeping information "on line" for each trial, which suggests a function similar to the second definition Baddeley and Hitch (1994) described, i.e., the concept that working memory may be conceptualized as a system that combines storage and processing of incoming information. On this basis, a wealth of information has been obtained concerning the anatomical basis of working memory in nonhuman primates, much of which is consistent with the findings in humans.

Many studies involving single unit recording and lesions of DLPC using delayed-response tasks have implicated the DLPC in working memory (Fuster, 1984; Goldman-Rakic, 1987). These tasks involve a temporal separation between the initial encoding of the information and the execution of the desired behavior based on the

temporarily stored information and subsequent cues. In an early study, Fuster (1973) found specific neurons in the prefrontal cortex that were differentially sensitive to the cue period, delay period, and the response period. The task Fuster used required animals to remember the location of food hidden behind an opaque screen.

Goldman-Rakic et al. (1990) reported similar results in tasks requiring delayed oculomotor responses from monkeys. These tasks required the animal to fixate on a point for 3-5 seconds after an initial target was presented and removed, prior to making a saccade to the location of the target. This task required the animal to hold the stimulus location "on line" since anticipatory saccades are prevented. Results indicated that there were individual neurons in the dorsolateral principal sulcus that showed either excitatory or inhibitory activity during each discrete phase of the task, e.g. the cue period, delay period, and the response period. In addition, there was neuronal activity related to combinations of the various phases. The neurons also were preferentially sensitive to particular orientations of the target cue. In an effort to rule out the possibility of the neuronal activity resulting from a simple motor set, the authors also required the monkeys to perform an anti-saccade task. This required the animals to respond in the opposite direction of the cue following the delay period. That required the animals to both hold the original

location "on line" and manipulate it in such a way as to determine the opposite direction. The authors found that two-thirds of the neurons that fired to a particular stimulus orientation in the conventional saccade task, also fired for the same stimulus orientation in the anti-saccade task. Other studies involving ablations, cooling, and metabolism monitoring of the DLPC have provided similar results with regard to the involvement of the DLPC in working memory (Bauer & Fuster, 1976; Friedman & Goldman-Rakic, 1994; Goldman & Rosvold, 1970; Goldman et al., 1971; Sawaguchi & Goldman-Rakic, 1994).

Neurons with similar firing patterns during similar oculomotor delayed response tasks have also been found within the caudate (Hikosaka et al., 1989). The authors note that the areas of the caudate which showed selective neuronal firing during memory portions of a saccade task were also the regions to which the DLPC has heavy projections, suggesting that the caudate may play at least a sequential role in memory, in that information appears to be sent through the caudate in the manner of other cortico-striato-pallido-thalamo-cortical loops. Hikosaka et al. (1989) postulated that interference with fronto-striatal connections may result in cognitive deficits. The SNr has also been shown to have neurons that appear to respond preferentially to memory-contingent visual saccades (Hikosaka & Wurtz, 1983). The authors suggested that the SNr may be the final stage of processing within

the basal ganglia, where sensory, motor, and cognitive functions are combined. Taken together, the similarity found between the patterns of neuronal firing in the DLPC and the basal ganglia suggest that they are part of the same processing system.

Overall, there appears to be a role for prefrontal cortex in working memory, as suggested by both functional neuroimaging and physiological studies performed with animals. Based on this information, and the connections between prefrontal cortex and the basal ganglia described previously, it is plausible that there are deficits in working memory in patients with PD. In order to examine the functional relevance of a working memory deficit in patients with PD, it may be necessary to examine an activity that has been proposed to utilize working memory, such as reading comprehension.

Sentence Processing and Comprehension

Martin, Shelton, and Yaffee (1994) proposed that sentence processing involves both semantic and phonological aspects of working memory, based on a study in which they were able to dissociate these concepts in two patients. The investigators performed a study using two brain damaged patients. A.B., who showed a deficit in short-term retention of semantic information, was operated on for a left frontal hematoma. A subsequent CT scan showed low-density regions in the posterolateral aspect of the left frontal lobe, and the adjacent anterior parietal

lobe. E.A., who showed a deficit in the short-term retention of phonologic information, experienced a stroke. A CT scan showed a lesion involving left temporal and left parietal lobes; specifically, the primary auditory cortex, Wernicke's area, and both superior and inferior parietal lobules showed evidence of involvement. In terms of span tasks, short-term memory testing revealed that A.B. showed a normal phonological similarity effect, and E.A. did not. In addition, A.B. showed superior recall for digits to E.A., a task that is largely phonological in nature. E.A. also showed a substantial advantage recalling words over nonwords. The authors also performed rhyme and category probe tasks in which the subjects were read a list and asked if a category or a word that rhymed with the probe had been on the list. E.A. performed better than A.B. on the category probes task, while A.B. performed better than E.A. on the rhyme probe task. The subjects also performed sentence repetition and sentence comprehension tasks, and showed deficits in the expected directions. A.B. was more successful in verbatim recall, and E.A. responded with many paraphrases, suggesting that she was relying more heavily on the semantic content of the sentences. In sentence comprehension tasks, A.B. scored significantly lower than E.A. when the amount of semantic information exceeded a critical level.

The authors' interpretation of these results was that working memory in sentence processing involves multiple

capacities, rather than a single capacity, and that there is some relation between the memory resources involved in span tasks and those involved in sentence processing. These capacities appear to be separate, rather than a single capacity that may be allocated to either type of processing as proposed by Just and Carpenter (1992). This is consistent with the results of Hulme et al. (1991) who showed both semantic and phonologic contributions to word span tasks. Martin and Romani also stated that good sentence comprehension demonstrated by patients with poor phonologic short-term memory suggests that syntactic and semantic processes are applied to each word as it is received. The authors employed the Martin and Saffran (1992) model in an effort to explain the results. They propose that activation spreads from phonological nodes to lexical nodes to nodes for semantic features. Activation also spreads backwards. Therefore, in normal subjects, persisting semantic activation may serve to maintain activation of the lexical and phonologic units. Better repetition of words than nonwords may be explained by the fact that lexical and semantic information in words helps to keep their phonological representation activated in a top down manner. It could be hypothesized that E.A.'s poor sentence repetition is due to a lack of sustained activation at the phonological level, while A.B.'s poor comprehension implies impaired activation at the semantic level. Other studies have also demonstrated intact

comprehension (Baddeley & Wilson, 1988; Martin, 1987 & 1993; Martin & Caramazza, 1982; Martin & Feher, 1990; Saffrin & Marin, 1975) and on-line semantic processing (Carpenter & Daneman, 1981; Tyler & Marslen-Wilson, 1977) without demonstrable phonologic short-term memory.

It is important to note that the patients described by Martin et al.(1994) had language deficits. They reported that A.B. had a dense global aphasia immediately following surgery, which resolved over several months into a mild aphasia with receptive and expressive components. His spontaneous speech was described as severely reduced, with well formed, short, sentences with apparent word finding difficulties. E.A.'s speech appeared less impaired. Despite the fact that she had lesions in primary auditory cortex, Wernicke's area, and superior and inferior parietal lobules, she was noted to have good speech expression with occasional phonological paraphasias on longer words. However, if language and working memory are conceptualized in neural network terms, then the same networks support both facilities. Thus deficits in specific language functions will go hand in hand with deficits in conceptualized types of working memory. Martin et. al (1994) proposed that these networks were dissociable, but were unable to provide evidence of semantic/phonologic network damage to components unique to working memory demands.

Deficits in the processing of syntax have also been proposed as playing a role in impaired sentence comprehension. Martin and Romani (1994) performed a study examining semantic and syntactic aspects of sentence comprehension within the context of working memory. The subjects included E.A. and A.B., whose deficits were described above, and M.W., who experienced a stroke in the left basal ganglia region. Following the stroke his comprehension was intact, and his spontaneous speech was characterized by word finding difficulties and mild dysarthria. M.W. did not appear to have any short-term memory deficit. The authors used a sentence anomaly task as a measure of retention for lexical-semantic information. In the task, the subjects made judgments about the appropriateness of sentences. The location of adjectives and noun phrases was varied. Some were canonical (traditional sequence) sentences, which allowed immediate integration of semantic information. Other sentences, because of their disorganized sequence, required semantic information to be held in short term memory in order for judgments to be made. On this task, A.B. (who was presumed to have a semantic working memory deficit) was impaired relative to controls and the other patients in his ability to make sentence anomaly judgments when unintegrated semantic information needed to be held in short-term memory. Martin and Romani also had the subjects perform grammaticality judgment tasks. These

required the patients to evaluate pronoun-case, noun-verb, and auxiliary-verb agreement. The number of words between the two target words varied between zero and three. A.B. was not impaired in this task, while M.W. did show some impairment. There was also a grammaticality judgment task which stressed memory by having a condition with added words between the target words. Once again, M.W. performed substantially worse than A.B. Despite the fact that M.W. appeared to have deficits in grammatical facility, the authors suggested that M.W. had difficulty maintaining incomplete syntactic structures, while A.B. was impaired in his ability to maintain unintegrated semantic information in short-term memory. They interpreted these results in the context of an interactive activation model similar to the model proposed by Martin and Saffran (1992). However, Martin and Romani propose a separate syntactic level of working memory. This referred to the development of syntactic structure on a word by word basis. As soon as information is available for linking word meanings together, propositions are developed. Syntactic working memory would be represented as a higher order function than either semantic or phonological working memory, meaning that intact semantic or phonological working memory is necessary but not sufficient for syntactic working memory. Therefore, word lists would only require the bottom two levels (phonological and semantic abilities), while for sentence

comprehension all four levels (phonological, semantic, syntactic, and propositional) may be important. Once again, however, the authors fail to consider what effect a compromised language processor may have for these memory tasks, as is possible in the patients used for this study. The authors fail to distinguish whether the deficits are due to deficiency of components unique to working memory or deficiencies in the phonological/semantic network.

To summarize, there appears to be a role for working memory in sentence comprehension. This may include elements of both semantic working memory and phonological working memory. Based on this conclusion, one would expect impairments in working memory to impact a task measuring sentence comprehension. If patients with PD do have a working memory deficit, it is possible that this may be evidenced in a task measuring sentence comprehension, and PD patients should show a pattern of deficits in studies examining PD, working memory and sentence comprehension. Additionally, PD patients do not have damage to language processors. Thus working memory capacity may be examined without the confound of working memory deficits implicit in processor dysfunction.

Parkinson's Disease, Working Memory, and Sentence Comprehension

In an effort to determine the nature of working memory, it may be helpful to further define specific constructs within the area of working memory

experimentally, such as the role of working memory in sentence comprehension. Patients with PD provide an opportunity to examine working memory and sentence comprehension, as the degenerative nature of the disease affects areas of frontal cortex through reciprocal connections with subcortical structures detailed above, and frontal cortex has been implicated as being important for working memory and sentence comprehension. While a variety of studies have suggested that individuals with PD are impaired on complex cognitive tasks in a manner similar to patients with frontal lobe damage, relatively few of these studies have closely examined the precise nature of the cognitive changes in patients with PD (Pirozzolo, Swihart, Rey, Mahurin, & Jankovic, 1993).

Multiple studies have employed the Wisconsin Card Sort Test (WCST) or similar tests of frontal function, with mixed findings in PD patients. Many have found impairments on these tasks (Bondi et al., 1993; Caltagirone, Carlesimo, Nocentini, & Vicari, 1989; Cooper, Sagar, Jordan, Harvey, & Sullivan, 1991; Flowers & Robertson, 1985; Lees & Smith, 1983; Gotham, Brown, & Marsden, 1988; Owen et al. 1993; Robbins et al., 1994; Sagar, Sullivan, Cooper, & Jordan, 1991; Taylor et al., 1986; Tsai, Lu, Hua, Lo, & Lo, 1994), while other studies have found little impairment on these types of tasks (Canavan et al., 1989; Cooper et al., 1992; Dalrymple-

Alford, Kalders, Jones, Watson, 1994; Pillon, Dubois, Ploska, and Agid, 1991). Within the studies that did find impairments, there was also variability with regard to number of categories achieved, total errors, and perseverative errors. There are several factors that may contribute to the heterogeneous nature of these results, including: disease duration, presence or absence of superimposed Alzheimer's disease, severity of dopamine depletion, distribution of pathology, and medications. Patients have also been shown to be impaired using other measures of frontal function, including the Stroop (Brown & Marsden, 1991) and verbal fluency tasks (Dalrymple-Alford et al., 1994; Levin, Llabre, & Weiner, 1987; Taylor et al., 1986). However, not all investigators have found impaired performance on verbal fluency (Bondi et al., 1993; Miller, 1985; Pillon et al., 1991; Tsai et al., 1994). Overall, these studies may be taken as being suggestive of frontal involvement in cognitive changes in patients with PD; however, the lack of consistent results suggests future research is necessary to determine what underlying cognitive and physiological deficits may explain the possible impairment.

The same variability has plagued studies that have examined memory in PD patients. While some authors have found impairments in spatial memory (Owen et al., 1993; Robbins et al., 1994; Sahakian et al., 1988; Taylor et al., 1986; Taylor, Saint-Cyr, & Lang, 1990; Tsai et al.,

1994), others have not (Caltagirone et al., 1989; Cooper et al., 1991; Cooper & Sagar, 1993). Similarly, variable results have been found with regard to short-term and long term verbal memory. While some authors find normal performance on short-term verbal memory as measured by woed list learning and story recall (Pillon et al., 1991), others find impairment (Cooper et al., 1991; Sagar, Sullivan, Gabrieli, Corkin, and Growdon, 1988; Sullivan, Sagar, Cooper, & Jordan, 1993; Taylor et al., 1986, 1990; Tsai et al., 1994). Long-term verbal memory follows a similar mixed pattern of results with regard to findings of normal performance (Taylor et al., 1986), and impairment (Cooper et al., 1991; Taylor et al., 1990).

While many of the preceding studies have tasks that may be conceptualized in terms of verbal working memory, relatively few experimenters have designed studies to specifically examine verbal working memory in PD patients. Goldman-Rakic (1987) described working memory as including the ability to hold information "on-line" while manipulating other information. Tasks requiring extensive manipulation of secondary information will place a greater demand on available working memory, thus making mild working memory deficits more apparent. Brown and Marsden (1991) examined working memory and found that PD patients showed a relatively greater increase in reaction time than normals when performing the Stroop at the same time as a resource demanding secondary task. They interpreted this

in terms of a central processing deficit in accordance with an impaired central executive (Baddeley and Hitch, 1994) central to working memory. Similarly, Dalrymple-Alford et al. (1994) also found that patients were impaired on a random pursuit motor tracking task while attempting to recall sequences of digits. The patients were not impaired relative to control subjects on either of the tasks when the tasks were performed individually. These authors also attributed the deficit to a defect in working memory and the central executive responsible for resource allocation. Cooper and Sagar (1993) found similar results following manipulation of attentional resources by comparing incidental to intentional spatial recall. However, the previous studies may also reflect deficits in ability to perform simultaneous tasks independent of any working memory requirement.

Further evidence for deficits in working memory in PD patients comes from short-term memory tasks in which distracters are presented during the interval between presentation and recall of stimuli. Sullivan et al. (1993) used a Brown-Peterson paradigm on never-treated, newly-diagnosed PD patients in which subjects counted backwards by three's following presentation of a consonant trigram. They also had subjects perform a non-verbal analog using Corsi blocks. The distraction task consisted of the examiner touching a finger on one hand of the subject, who was then required to touch the same finger on

the other hand. Results for the verbal tests indicated that PD patients were impaired in the distracter-filled condition, but normal in the distracter-free condition. Results for the non-verbal tests showed the opposite pattern of performance, with PD patients normal during the distracter-filled condition, and impaired on the distracter-free condition. The authors did not offer an explanation for these contradictory results, other than to attribute deficits in both modalities to faulty encoding. The authors did note that performance in both modalities was correlated with score on a dementia rating scale. Thus global dementia may have impacted language functions in a different manner than visual functions. This paradigm requires working memory in that individuals have to keep information in mind while performing another task. However, since the items to be remembered have little meaning, semantic working memory is not being tapped.

Deficits in memory for temporal order is another cognitive area that has been linked to both PD and frontal lobe deficits, further implicating possible frontal lobe dysfunction in PD. As a task, judgment of temporal order presumably requires working memory, since information must be constantly updated as new material is presented. For instance, a subject may be presented a list of five words, and then shown two words from the list and asked which word came first. The subject must recall the words on the list in the correct order to make a judgment. A variety

of studies have shown that patients with frontal lobe damage have difficulty making relative-recency decisions about items presented sequentially (Eslinger & Grattan, 1994; McAndrews & Milner, 1991; Shimamura, Janowsky, & Squire, 1990). Sagar et al. (1988) compared PD patients with normal controls and Alzheimer's patients on a task requiring either recognition or temporal judgment of sequentially presented stimuli. PD patients were impaired in the verbal recency condition with preserved recognition of stimulus content. The fact that newly diagnosed patients showed impairment suggests that this task is sensitive to early deficits associated with PD. In addition, ordering presumably has a higher working memory requirement since a subject must remember where items were on a list rather than simply recognize if the words were on a list. Bondi et al. (1993) reported similar results with PD patients who were medicated and classified as either Stage II or Stage III PD (Hoehn & Yahr, 1967). Sullivan and Sagar (1989) also found the same pattern of results with a non-verbal temporal ordering task. Vriezen and Moscovitch (1990) found the same pattern of results with PD patients, who had been taking levodopa, on both verbal and non-verbal temporal ordering tasks.

Although it is commonly assumed that the cognitive deficits found in PD patients are due to DA depletion, it is possible that other neurotransmitter systems may be affected sufficiently to cause cognitive deficits.

However, in comparison to the number of studies in general using PD patients, relatively few studies have attempted to directly examine the role that DA plays in cognition, and the results of these studies have been mixed. However, these studies are the most relevant to the role of subcortical structures as compared to cortical structures in cognition, as the striatum is more dopamine dependent than the relevant cortical structures. Manipulation of DA levels is one method to tease apart cortical and subcortical deficits in PD. In addition, manipulation of DA levels allows one to begin to disentangle the problem of dissociating working memory deficits from structural damage to the memory networks themselves. If the memory networks are intact, but are being negatively affected by a reduction in DA, replacing the DA in the system should result in normalization of performance.

Akinesia and bradykinesia are primary problems in patients with PD, and several studies have examined the degree to which complex movements and choice based reaction times (which presumably are more dependent on cognitive processes than simple movements and simple reaction times) may be differentially affected by DA levels. Results with such paradigms have been mixed. Pullman, Watts, Juncos, Chase, and Sanes (1988) examined simple and choice reaction times in PD patients while levodopa levels were controlled. The PD patients were

slower than controls in both high and low levodopa conditions. They were relatively more impaired in the choice reaction time, where they had to choose between wrist extension or flexion, when they were on low levels of levodopa than when they had high levels of levodopa. There were no significant differences in reaction times on the unidirectional task, regardless of levodopa levels. However, other studies have not found a relationship between simple and complex reaction time and levels of dopaminergic medication (Girotti et al., 1986; Jahanshahi, Brown, & Marsden, 1992; Malapani et al., 1994; Pullman, Watts, Juncos, & Sanes, 1990). These differences in results may be related to the level of movement complexity, as Benecke, Rothwell, Dick, Day, and Marsden (1987) found differentially greater improvement in movement times in complex compared to simple movements with levodopa treatment.

The relationship between akinesia, bradykinesia, and higher cognitive function is unclear, and several studies have attempted to directly examine the relationship between DA and cognition. Pillon, Dubois, Bonnet et al. (1989) performed a study evaluating the relationship between levodopa and higher cognitive functions. Motor disability was evaluated using the modified Columbia scale and the average score of the PD patients was 29.9/92 when off medication, and levodopa improved this an average of 54.1%. The tests included the following: a 15-object test

of superimposed line drawings; digit span, similarities, and arithmetic subtests from the Wechsler Adult Intelligence Scale (WAIS); the Wechsler Memory Scale (WMS); and the Raven 47 colored progressive matrices (PM-47). Results indicated the PD patients scored significantly lower than controls on all tasks. The authors combined the remaining tests into a deterioration index, and there was no significant change in the index as a result of levodopa treatment. The authors did not report a comparison of types of errors the PD patients made when on and off medication.

Pillon, Dubois, Cusimano et al. (1989) studied cognition in relation to motor disability in patients with PD. The average basal motor score on the modified Columbia scale was 28.9 when off medication, and 13.9 when on medication. Tests included, digit span, similarities, and arithmetic from the WAIS, the PM-47, the WMS, the WCST, and verbal fluency. Results indicated that the patients' performance on the memory and intelligence tests were within normal limits for age matched controls individually, but when the tests were combined into a deterioration index, they were below what would be expected. There was no correlation between levodopa treatment and the scores on any of the neuropsychological tests. The authors reported that cognitive impairment was not correlated with akinesia and rigidity, but significant correlations were found between axial symptoms, such as

gait disorder and dysarthria. The authors interpreted these correlations as evidence for a role of non-dopaminergic neuronal systems in the cognitive impairment found in PD. The authors based this on the fact that they have generally found good responses to levodopa treatment for akinesia and rigidity, but poor responses for symptoms such as gait disorder and dysarthria. However, these correlations are based on an absence of change in the domains measured, and it is possible the cognitive tests were not sensitive to cognitive dimensions that may be affected by DA and levodopa. In addition, they did not report differences between delayed and immediate recall measures.

Several studies have found relationships between cognitive functions and levodopa treatment. Lange et al. (1992) compared the performance of ten patients with PD on measures of visual learning, memory, planning, and attention while both on and off levodopa. The patients' severity was rated according to the Hoehn and Yahr (1967) scale of disability, and six of the patients were rated at level III, three were rated at level IV, and one was rated at level V. Patients were tested on computerized measures of short term spatial span (e.g. Corsi Block Tapping Test), spatial working memory, planning ability (a task similar to the Tower of London), visual discrimination/attentional set shifting (using principles similar to the WCST), and visual memory/learning. Results

indicated that patients performed significantly better on measures of accuracy and latency on the planning task when on levodopa than when not taking the drug. Patients tested while taking levodopa also performed significantly better on the visual discrimination/attentional set shifting task, the spatial working memory task, and spatial span. The authors proposed that levodopa withdrawal selectively impaired tasks sensitive to frontal lobe damage (Lange, Paul, Robbins, & Marsden, 1993). Working memory deficits may have contributed to some of these deficits.

Gotham et al. (1988) chose to examine capacities which have been shown to be affected by frontal lobe dysfunction, based on subcortical and DA connections which degenerate in PD. Sixteen PD patients were given the following tests while they were both on and off levodopa: the Paced Auditory Serial Addition Task (PASAT); the WCST; the Visual-Visual Conditional Associative Learning Test, which required learning arbitrary associations between pairs of visual stimuli; verbal fluency; and Subject Ordered Pointing Tasks, which require organization of a sequence of pointing responses. Sixteen control subjects also received a single presentation of the same tests. The authors made both within group comparisons (patients on and off medications) and between group comparisons (patients on and off medication compared to controls). Results indicated there were no significant differences on

the tests when PD patients were on levodopa compared to when they were off levodopa. However, when compared to the control subjects, PD patients were significantly more impaired on verbal fluency when off levodopa than when on levodopa. However, one element the authors did not comment on was the motor component inherent in speaking, and the possibility that motor difficulties may have decreased the number of words the PD patients could verbalize in one minute. When on medication, the patients were significantly worse than controls on the conditional learning test and the subject-ordered pointing task. The PD patients performed more poorly than controls on the WCST both on and off levodopa. The authors proposed two elements which contributed to the enhancement and impairment of functions associated with the frontal lobes. They noted that each of the tests probably taps different aspects of frontal function, and also that DA may have different effects on these cognitive functions. However, the authors acknowledge the difficulty in accurately defining what these different aspects of frontal function may be. They pointed out that DA levels may differentially affect regions associated with verbal fluency and regions associated with self-ordered pointing tasks and visual conditional learning. They proposed that one area may be more DA depleted than the other, and DA stimulation may result in one area being optimally stimulated, while another area may become over stimulated.

The authors acknowledged that this may be an oversimplification and may fail to take synaptic characteristics such as autoreceptors into account, but stress that DA appeared to impact cognitive functions associated with these tests.

Lange et al. (1992) attempted to explain the apparent difference in results between the two similar studies based on differing methods of statistical analyses in the two studies. The conditional associative learning results and the subject ordered pointing results appeared to differ between the two studies. Upon closer examination, however, in Gotham et al. (1988) the PD patients also were not significantly different when compared to each other (as was also the case in Lange et al., 1992). The differences between the on and off conditions were revealed based on separate comparisons of the on group to the control group, and of the off group to the control group.

Mohr, Fabbrini, Ruggieri, Fedio, and Chase (1987) examined the cognitive effects of levodopa in eight PD patients, with an unmedicated range of II to IV on the Hoehn and Yahr (1967) scale. In addition, eight normal control subjects also underwent testing. Patients' levels of levodopa, for the purpose of measuring levodopa levels during the off period, were evaluated through blood testing. Tests that were compared during on and off periods included verbal fluency, Logical Memory, Paired

Associates, and visual form discrimination (using embedded figures). Results indicated that patients' scores improved on delayed Logical Memory and delayed Paired Associates during the levodopa stimulated state, while the other test scores remained stable. The authors suggested that the selective effects on delayed memory resulted from the fact that delayed memory may require more effortful processing. The authors also note that the functions significantly improved by levodopa therapy were also those that were most impaired relative to the control group.

Studies employing single-photon emission computed tomography (SPECT) and positron emission tomography (PET) techniques have also suggested that DA plays an important role in cognitive impairments associated with PD; however, there do not appear to be imaging studies involving DA manipulation, which would provide the most relevant information concerning the role of DA in cognition in PD patients. Démonet et al. (1994) measured the rCBF with SPECT for 18 PD patients in the early stages of the disease (Hoehn and Yahr stages I-II) and 20 normal controls during rest, passive listening, and memorization conditions. When the listening condition was compared to the memorization condition, normal subjects showed an increase in activation in the left posterior-inferior frontal region (roughly Broca's area), left anterior-middle frontal region (dorsolateral prefrontal cortex), left superior-middle temporal region (roughly Wernicke's

area), and left lenticular and thalamic regions. The PD patients showed a completely different pattern of activation, with significant bilateral activation in only the superior frontal region, and thalamus, and activity in the right lenticular region and right dorsolateral prefrontal cortex. The authors speculated that this was a breakdown of the articulatory rehearsal system in the PD patients, and suggest that the superior frontal activation results from PD patients relying more heavily on semantic cues from the information. It is difficult to determine what underlying pathology may account for this discrepancy in terms of cortical compared to subcortical structures, as DA levels were not manipulated in the design. However, results from Sawada et al. (1992) suggest that the rCBF differences may be specific to cognitive activities, as they found no differences between PD patients and normal controls during a 60 minute rest period.

Playford et al. (1992) used PET technology to measure activity during motor tasks in PD patients and controls. The tasks included a rest portion in which they simply heard a tone, a repetitive task where the subjects moved a joystick forward each time they heard a tone, and a free-selection task where subjects moved a joystick in any one of four possible directions at the sound of a tone. It is important to note that on the free selection task they were told to avoid repetitive sequences, which would result in the employment of working memory in an effort to

remember all previous patterns of movement, so as to not repeat any previous sequence. When the rest condition was compared to the free choice condition, normals showed significant increases in activity in the left primary sensorimotor cortex, left premotor cortex, left putamen, right dorsolateral prefrontal cortex, and bilateral activation of supplementary motor area, anterior cingulate area, and parietal association areas. The PD patients only showed significant increases in activity in left sensorimotor and premotor cortices. The authors suggested that the impaired activation may contribute to PD patients' difficulty in initiating movements. The lack of activity in higher cortical areas also suggests an impairment in the more cognitive components of the task.

In addition to the impairments that have been found within specific cognitive domains in PD patients, impairments in the more generalized cognitive domain of sentence comprehension have also been reported. Once again, however, there do not appear to be any studies in the literature involving DA manipulation in PD patients, which would provide information about the underlying causes of the sentence comprehension deficits. Grossman et al. (1991) designed a study to measure sentence comprehension, while manipulating syntactic complexity within the sentences, in 22 patients with PD. All patients were at either stage I or II on the Hoehn and Yahr (1967) scale, with the exception of one who was at

stage III. The sentences included simple (e.g. "The eagle chased the hawk"), subordinate with a relative clause at the end of the sentence (e.g. "The eagle chased the hawk that was fast"), and subordinate with a relative clause in the middle of the sentence (e.g. "The eagle that chased the hawk was fast"). The subjects then received a simple probe about each sentence, such as "What did the chasing?" The authors also manipulated the voice correspondence (active vs. passive) between the target sentence and the probe. The sentences were also varied in their semantic constraint, in that half the sentences contained nouns that could be exchanged (e.g. "The eagle chased the hawk"), and half the sentences contained nouns that could not be exchanged (e.g. "The eagle chased the worm"). Results indicated that the PD patients were significantly worse on the subordinate and center-embedded sentences than both controls and their own performance on the simple sentences. The patients were not significantly different on the simple sentences. The PD patients were also significantly impaired relative to controls when voice correspondence between the sentence and the probe did not agree. Finally, there was also a difference in semantic constraint, as patients performed significantly worse on nonconstrained sentences compared to patients' performance on constrained sentences. The authors proposed that this was a language specific deficit, and was not related to impairments in memory or attention, based on concurrent

memory testing they performed. However, the memory testing consisted of a digit span task and recall of three words at one and five minutes. The more complex sentences required more complex processing, and required that more information be kept in working memory as the sentences were processed. If the PD patients had a deficit in verbal working memory, it may produce the same pattern of results. Deficits in working memory may not have been revealed by the memory testing performed in this study.

Grossman, Carvell, Stern, Gollomp, and Hurtig (1992) performed an extension of the previous study using the same sentences and a similar sample of patients. They replicated the results of the previous study with regard to the performance of the PD patients on sentence comprehension. In addition, they administered further measures of attention and memory in an effort to evaluate the possible role these factors may play in the patients' impaired sentence comprehension. The attention measures included orientation, digit span, calculation of four arithmetic word problems, and the repetition of three words. Memory measures included recall of three words at one and five minutes, recall of seven presidents, and production of items to a supraordinate target category. The authors found that the PD patients were not significantly worse than controls on the memory measures. However, impaired working memory may still have been playing a role in the impaired sentence comprehension as

none of the memory or attention tasks addressed this possibility. The authors performed a final manipulation in which they varied the distance between words that were relevant to the probe, reasoning that this would place increased demands on memory. There was no difference between the PD patients and the controls on this task. However, each sentence was read twice to the subjects, and they were allowed to request as many repetitions as they required. This would appear to minimize the demands made on working memory necessary for sentence comprehension.

Grossman, Crino, Reivich, Stern, and Hurtig (1992) examined rCBF in PD patients and normals while at rest and while answering questions about sentences. There were three conditions in which subjects monitored visually presented sentences for the letter "k", for an adjective, or for a female agent. Results for normal patients when the letter detection task was compared to the other tasks showed bilateral activation of the anterior cingulate and lateral temporo-occipital cortex, and left-sided activation of middle and inferior frontal cortex, superior temporal cortex, caudate, and thalamus. The PD patients did not show any changes in activity when the letter detection task was compared with the other two tasks. The authors reported these results were consistent with reports of hypometabolism found during relative resting states in other activation studies of PD patients (Grossman et al., 1993; Sawada et al., 1992). This study

suggests that PD patients' diminished level of brain arousal measured by activation studies may allow them to perform normally on tasks that have relatively low demands; however, as cognitive demands rise, PD patients may show greater levels of impairments. However, the authors do not discuss methodological concerns related to comparing tasks to resting states. It may be more appropriate to compare activation tasks to activity during suitable control tasks.

Based on the above information, the purpose of the present study is to explore the performance of PD patients on working memory and sentence comprehension tasks in differing states of DA depletion. PD patients were chosen because they have a pattern cerebral dysfunction that is manipulable by changing dopamine levels. Because of the prominent role of dopamine in basal ganglia function, it can be assumed that manipulation of dopamine levels will change cognitive functions if the basal ganglia play a significant role in such functions. Dopamine is assumed to play a less important role in cortical than in basal ganglia processing, allowing for the relative isolation of basal ganglia functions through the manipulation of dopamine levels. This allows examination of the role of the basal ganglia in linguistic working memory. Abundant evidence implicates frontal lobe systems in working memory processes and implicates the caudate nucleus in frontal lobe system anatomy and function. PD is associated with

loss of dopaminergic input to the caudate. The central hypothesis is that caudate dopamine deficiency in patients with PD will cause deficits in working memory by virtue of associated dysfunction in dorsolateral prefrontal cortices connected to the caudate nucleus. By studying patients both on and off dopaminergic medication, it should also be possible to discriminate working memory deficits attributable to caudate dysfunction from working memory deficits attributable to cortical disease. A second hypothesis is that semantic working memory and working memory involving syntactic components will be more impaired than phonological working memory in patients with PD off dopaminergic medication because of the particular role of dorsolateral prefrontal cortex in semantic and syntactic processes.

Hypotheses

Specific hypotheses for comparisons of PD patients on and off medication include the following:

1) PD patients will perform more poorly on a semantic working memory task when off medication than when on medication. PD patients will not differ significantly on a phonological working memory task when on and off medication conditions are contrasted. PD patients have been shown to have deficits related to frontal lobe dysfunction. It has been suggested that semantic processing of information requires a higher level of frontal lobe involvement than does phonological processing

of information. Thus, frontal lobe dysfunction, as experienced by PD patients, may affect semantic memory to a greater degree than phonological memory.

2) Based on the relationship between working memory and sentence comprehension, PD patients on medication will make fewer errors than patients off medication on sentences of medium and high difficulty on a measure of sentence comprehension including both semantic and syntactic elements.

3) Sentences that have greater syntactic requirements will be more difficult than sentences that have minimal syntactic requirements regardless of medication status due to overall larger working memory requirements demanded by complex syntax.

4) PD patients will experience a greater drop in performance, when in the off medication condition, on sentences that require syntactic understanding of information than on sentences that require semantic understanding of information. Overall working memory requirements are larger for sentences requiring syntactic understanding, and it has been hypothesized that PD patients have deficits in working memory.

5) There will be no differences in self-reported levels of depression for PD patients when on medication compared to off medication.

6) There will be no differences on a series of control tasks measuring naming, embedded figure

discrimination, and wordlist repetition. These were included in an effort to show deficits when patients are off medication are specific and not related to generalized cognitive decline. These abilities have generally been shown to be intact in PD patients, although there are exceptions in the literature.

A control group of healthy subjects was included to contrast deficits specifically related to basal ganglia dysfunction (controlled through DA manipulation) with deficits related to incipient Parkinsonian dementia. Specific hypotheses for healthy control subjects compared to PD patients include the following:

1) PD patients on medication and control subjects will not differ on a measure of working memory, while PD patients off medication will be impaired on the semantic, but not phonological working memory measure relative to controls. As working memory has been proposed to be affected by basal ganglia functioning, providing DA replacement through medication is hypothesized to bring basal ganglia functioning back to a baseline level. PD patients have been shown to have deficits related to frontal lobe dysfunction, and frontal lobe dysfunction may affect semantic memory to a greater degree than phonological memory. There will be no difference between PD patients on medication and controls due to the replacement of DA.

2) Control subjects will make fewer errors than patients when on and off medication on a measure of sentence comprehension. This difference will be present on sentences that have high syntactic requirements as well as on sentences with minimal syntactic requirements. Previous research has suggested that PD patients have deficits in sentence comprehension regardless of medication status, and this may reflect incipient Parkinsonian dementia.

3) Sentences that have greater syntactic requirements will be more difficult than sentences that have minimal syntactic requirements regardless of medication status due to overall larger working memory requirements demanded by complex syntax.

4) PD patients will have significantly elevated levels of self-reported depression relative to controls regardless of medication status, as PD has been associated with increased levels of depression.

5) There will be no differences between PD patients and controls on a series of control tasks measuring naming, embedded figure discrimination, and wordlist repetition regardless of medication status. These were included in an effort to show deficits in PD patients are specific and not related to generalized cognitive decline. These abilities have generally been shown to be intact in PD non-demented PD patients, although there are exceptions in the literature.

METHOD

Subjects

Subjects consisted of 14 patients diagnosed with idiopathic Parkinson's disease recruited from area support groups for individuals with Parkinson's disease and their families. A similar number of age- and education-matched neurologically intact subjects recruited from local volunteer organizations served as a control group. Consent to participate in the study was obtained after full disclosure of the study's purpose, risks, and potential benefits. The study was monitored by the Institutional Review Board (IRB) of the University of Florida. All subjects had been receiving levodopa treatment for at least three years. Potential subjects were excluded from the study if they had any of the following: history of psychiatric illness, history of drug abuse, history of brain damage, history of alcohol abuse, or evidence of dementia. Two PD subjects and one control subject were excluded due to failure to understand instructions for particular tasks, despite passing screening criteria.

Test Instruments

Mini-mental state. To screen for dementia, patients received the Mini-Mental State Exam (MMSE; Dick et al., 1984; Folstein et al., 1975) prior to testing. Scores of 25 or below were considered to indicate significant cognitive impairment and resulted in exclusion from the study.

Word span task. Each subject's word span was assessed using word lists developed for this project. All words used during the development of the list were equated for imageability and concreteness. In the task, words are read aloud, and subjects attempt to recall the words on each list in the order of presentation. Subjects' word span was defined as the list length at which they could recall all words on at least 2 of 4 word lists in the correct order. Word lists ranged in length from 4 to 7 words. Subjects were required to have a word span of at least four words. Two PD subjects were excluded from the study due to insufficient word span recall scores. This measure was included to control for general working memory capacity, related to premorbid abilities as well as degree of cortical disease.

Working memory task. Working memory was assessed using a measure developed for this project. The measure consists of two components. One component measures phonological contributions to working memory ("phonological working memory"), while the other measures

semantic contributions to working memory ("semantic working memory"). Three to seven words are read aloud to a subject, following which the subject counts backwards by two's from a preset number. Three cues are then presented one at a time to the subject. In the phonological cue condition, the cues consist of the examiner stating a word that rhymes with one of the words on the list, e.g. "Rhymes with frog." In the semantic cue condition, the examiner states the supraordinate category of one of the words on the list, e.g. "A type of animal." The subjects respond verbally to each cue prior to receiving the next cue. For each list read to the subject, the subject received either three semantic cues, or three phonological cues, depending on the cue condition.

In addition, in an effort to ensure that subjects biased their encoding toward the relevant strategy, patients monitored phonological lists for the sound "b", and the semantic lists for "something that is edible." They were asked to raise their finger each time they heard the phoneme "b" on the phonological list, or something edible during the semantic list. Each form of the test has the same number of edible items and "b" phonemes on both the semantic and phonological versions.

Prior to performing the task, each patient was screened with a series of 10 rhyming questions and 10 semantic questions with minimum memory requirements, to

ensure that patients were able to recognize both rhymes and semantic categories.

There were twenty lists, each having a maximum of 7 words. Within each testing session, each subject received 10 of the lists in the semantic form, and the other 10 lists in the phonological form. The order of list presentation and cue condition was counterbalanced across sessions. The number of words presented during the working memory task was based on the subjects' performance on the span task described above, with each subject receiving one less word than they achieved on the span task prior to administration of the working memory task. Thus, each subject had to achieve at least four words during the word span task in order to be included in the study. All words on the lists were equated for levels of imageability and concreteness (Toglia & Battig, 1978), in addition to having a minimum number of potential rhyming words.

Sentence comprehension task. Sentence comprehension was measured using a modified version of a task described by Grossman et al. (1982). The sentences consisted of target sentences, each of which was followed by a question (e.g., "The lion chased the tiger. What chased?"). Two factors were manipulated within the sentences: a "syntactic/semantic" factor and a difficulty factor.

The first factor is the syntactic/semantic factor, in which understanding and recall of exact sentence syntax is

necessary for a correct response for 1/2 of the sentences (e.g. "The eagle chased the hawk. What chased?"), while simple recall of semantic elements is necessary for the other 1/2 of the sentences (e.g. "The truck hit the tree. What hit the tree?"). Thus, in one type of sentence, it is semantically impossible to reverse the subject and object, therefore only semantic information is necessary. In the other type of sentence, the subject and object can be reversed, therefore syntactic comprehension is necessary. Thirty-six sentences of each type were presented. This manipulation was performed in an effort to differentiate if the suspected deficit in sentence comprehension seen in PD patients is due to difficulty with semantic working memory or difficulty with syntactic working memory.

The second factor that was manipulated was the level of difficulty. In those sentences where correct responses to probes depended on recall of syntax, difficulty was manipulated through variations in a subordinate clause, while keeping the number of semantic elements constant. In the lowest level of difficulty there was no subordinate clause (e.g. "The van hit the blue truck. What was hit?"). In the medium difficulty level, a subordinate clause was placed at the end of the sentence (e.g. "The skunk chased the porcupine that was hungry. What chased?"). In the high difficulty level, the subordinate

clause was placed in the middle of the sentence (e.g. "The cow that chased the donkey was angry. What chased?").

In those sentences in which recall of semantic elements was sufficient to respond correctly to the probe, difficulty level was manipulated by increasing the number of semantic elements. In the simple difficulty level there were three semantic elements (e.g. "The cat slapped the purple yarn. What slapped?"). In the medium difficulty level there were six semantic elements per sentence (e.g. "The playful silly cat popped the green round balloon. What popped?"). In the high difficulty level there were nine semantic elements per sentence (e.g. "The sleek, fast, greyhound and the fat, slow, turtle followed the long, winding, trail. What was winding?"). Probes were defined to reinforce ease of recall from semantic elements to further distinguish between the semantic and syntactic sentences. For example, turtles may theoretically be described as fast or sleek, but may not be described as winding.

There were 24 sentences at each difficulty level. The answer to the probe was evenly divided between the subject and the object. The difficulty manipulation was chosen due to the fact that published studies (Grossman et al., 1991; Grossman et al., 1992; Grossman et al, 1993) and pilot data have suggested that both normal controls and PD patients make more errors on more complex

sentences. The same sentences were used for all administrations.

Boston Naming Test. Naming was assessed using a modified version of the Boston Naming Test (BNT; Kaplan et al., 1983) in which individuals name drawings. In each testing session, every other item from the BNT was presented in order to provide alternate forms between the two testing sessions. Basal and ceiling levels described in the manual were not used in an effort to increase reliability, thus each subject received 30 pictures per session.

Embedded figures. A modification of an embedded figures task (Poppelreuter 1914-1917) was given in which patients were asked to name each of several overlapping figures on a stimulus card. Four cards with 3 to 5 figures per card were presented. Both number of correct responses and total time to name the items were measured. It was hypothesized that there would not be differences when the patients were on medication compared to when they were off medication (Pillon et al., 1989). This task was given as a control task in an effort to show that deficits when the patients were off medication, were relatively specific and not due to a generalized cognitive decline.

Geriatric Depression Scale. Depression is a common feature in patients with PD (Cummings, 1992). Although results are variable regarding the relationship between the effects of depression on cognitive performance in PD

(Cummings, 1992; Gotham et al., 1986; Rogers et al. 1987; Starkstein et al. 1989), it was important to measure patients' level of depression to explore any variations when on medication compared to subjects when off medication. This was accomplished through administration of the Geriatric Depression Scale (GDS: Brink et al., 1982). It is a 30-item scale constructed to not be highly sensitive to increased somatic complaints associated with the elderly, and has been shown to be reliable and valid when used with the elderly (Yesavage et al., 1983).

Unified Parkinson's Disease Rating Scale. Subjects' motor disability was assessed by a trained examiner prior to administration of cognitive measures using the motor exam of the Unified Parkinson's Disease Rating Scale (UPDR; Fahn, Elton, & Unified Parkinson's Disease Rating Scale Committee, 1987). The motor exam of the UPDR allows rating of speech, facial expression, resting tremor, action tremor, rigidity, manual dexterity, posture, gait, and balance. Each ability is rated from 0 to 4 based on specific criteria, with higher scores indicating greater symptom severity.

Procedure

Subjects were recruited from area PD support groups. PD patients were tested in their homes in both an "on" state, within 1 to 2 hours of their morning dose of anti-parkinsonian medication, and in an "off" state, in which patients were tested prior to taking their first dose of

anti-parkinsonian medication, with a minimum delay of 12 hours since the last dose. The order of "on" and "off" testing was counterbalanced across subjects, as was the administration of test instruments with alternate forms. The order in which the tests were administered was identical for all sessions.

Control subjects were recruited from local volunteer organizations. They were tested in homes and at a local community center. The control group was matched to the experimental group on the basis of age, education, and gender.

RESULTS

Table 1 lists demographic data and descriptive statistics for participants in the study. Two-tailed t-tests with an alpha level of .05 revealed no significant differences between the control group and the PD group in age or education.

Table 1

Demographic Data for Parkinson's Patients and Controls

	PD Patients		Controls			
Variable	*M*	*SD*	*M*	*SD*	*t*	*p*
Age	69.9	6.97	70.7	5.39	0.33	>.05
Education	13.4	3.46	14.2	3.33	0.61	>.05
Park Yrs	8.14	3.57	N/A	N/A		

Note. Park Yrs = # of years since PD patients began taking anti-parkinsonian medication.

First, the results from PD patients on medication will be compared to those from PD patients off medication. Subsequently, the results from the PD patients will be compared to those from control subjects. An alpha level of .05 (two tailed test) was used for all statistical tests unless otherwise noted.

Repeated measures ANOVAs were used in assessing medication effects. Parkinsonian patients had significantly lower UPDR ratings when on medication (M = 16.21, SD = 10.46) than when off (M = 24.07, SD = 10.61) medication, $t(13) = 4.29$, $p = .001$). GDS scores were no different on medication (M = 7.71, SD = 6.44) than off medication (M = 7.71, SD = 6.07), $t(27) = 0.00$, $p = 1.00$. This supports the hypothesis that depression would not be affected by a 12-hour hiatus in dopaminergic medication. Therefore, depression was not considered as a factor in subsequent on/off comparisons. MMS scores were no different on medication (M = 28.57, SD = 1.22) than off medication (M = 28.79, SD = .97), $t(27) = 0.76$, p = 0.46.

The results on the word span task, the score on the BNT, and the score on the embedded figures task were not expected to be affected by medication status. See table 2 for descriptive statistics for the general cognitive measures and the working memory tasks. A 2 x 2 (order x medication status) MANOVA revealed no significant interaction $F(6, 48) = 1.01$, or significant main effect

for order $F(6, 48) = .93$, or medication status $F(3, 23) = 2.13$. Subjects on medication ($M = 15.50$, $SD = .95$) scored better than subjects off medication ($M = 15.14$, $SD = 1.03$) on the embedded figures task $F(2, 25) = 4.17$, $MSE = .17$, $p = .052$. This medication effect was unexpected. However, the lack of a medication effect on word span or the BNT is consistent with hypotheses.

The working memory task was first analyzed with a 2 x 2 x 2 (condition x medication x order) repeated measures ANOVA. Results (see table 2 for descriptive statistics) indicated no significant interactions or main effects. As specific hypotheses were proposed for each working memory task, the data were also analyzed with separate t-tests for order and both conditions. None of these analyses were significant (see table 3). These analyses did not support the hypothesis that there would be an interaction, with subjects performing significantly more poorly on the semantic task when off medication than compared to the phonologic task when off medication. In addition, the hypothesis that subjects would have overall lower scores in terms of total items recalled when off medication than when on medication was not supported. It was also proposed that subjects would perform more poorly on the semantic working memory task than on the phonological working memory task, and this was not supported.

Table 2

Descriptive Statistics for Cognitive Measures

	PD On		PD Off		PD Diff		Control	
Variable	M	SD	M	SD	M	SD	M	SD
MMS	28.6	1.22	28.8	0.98	-0.21	1.05	29.0	0.78
GDS	10.4	7.48	10.4	6.80	0.00	2.29	5.0	3.78
BNT	26.2	3.17	25.9	3.50	0.35	2.47	27.6	2.06
Emb Fig	15.5	0.85	15.1	1.03	0.36	0.84	15.2	0.80
Span	4.4	0.51	4.4	0.50	0.00	0.47	4.57	0.51
WM Phon	11.6	4.32	10.3	4.41	1.35	3.56	12.0	3.33
WM Sem	12.0	5.02	12.8	5.49	-0.78	4.32	15.2	4.41

Note. PD On = Parkinson's patients on medication; PD Off = Parkinson's patients off medication; PD Diff = difference between Parkinson's patients on and off medication; Control = control subjects; MMS = Mini-Mental Status Exam; GDS = Geriatric Depression Scale; BNT = Boston Naming Test; Emb Fig = Embedded Figures Test; Span = Word span length; WM Phon = phonological working memory task; WM Sem = semantic working memory task

The sentence comprehension task was first analyzed for overall effects of medication status on sentences of medium and high difficulty using t-tests for the a priori hypotheses. T-tests did not approach significance and

revealed no differences between medication conditions (see table 3).

Table 3

T-tests of Working Memory and Sentence Comprehension Measures for PD Patients On versus Off Medication*

		PD On		PD Off			
Variable	df	M	SD	M	SD	t	p
WM Phon	13	11.6	4.32	10.3	4.41	1.42	.18
WM Sem	13	12.0	5.02	12.8	5.49	-0.68	.51
Syn Med	13	1.21	1.48	1.43	1.22	0.76	.46
Syn Com	13	3.07	1.44	2.86	1.66	-0.51	.62
Sem Med	13	0.64	1.01	0.79	1.25	0.43	.67
Sem Com	13	2.64	2.13	2.71	1.77	0.20	.84

Note. PD On = Parkinson's patients on medication; PD Off = Parkinson's patients off medication; WM Phon = phonological working memory task; WM Sem = semantic working memory task; Syn = Syntactic sentence condition; Sem = Semantic sentence condition; Sim = Simple; Med = Medium; Com = Complex; *working memory scores are # correct, sentence scores are # of errors;

In order to explore interactions between the various factors, a 3 x 2 x 2 x 2 (difficulty x sentence structure

x medication x order) ANOVA, with order a between subjects factor, and the other factors all within subjects. See tables 4 and 5 for descriptive statistics for the sentence comprehension task on the first and second task administrations. Results revealed a significant 4-way interaction between sentence difficulty, sentence structure, medication status, and order, $F(4, 50) = 3.83$, $p < .01$. In addition, there was an interaction between sentence difficulty and sentence structure, $F(2, 24) = 6.01$, $p < .01$, with the syntactic sentences of medium difficulty being more difficult than the semantic sentences of medium difficulty. There were main effects for sentence difficulty, $F(2, 25) = 55.1$, $p < .01$, with all three levels of difficulty being significantly different from each other, and for sentence structure, $F(1, 25) = 4.83$, $p < .05$., with participants doing more poorly on syntactic sentences than on semantic sentences.

Table 4

Descriptive Statistics for Sentence Comprehension Errors on First Administration

		PD On		PD Off		Control	
Type[a]	Diff[b]	M	SD	M	SD	M	SD
Syn	Sim	0.14	0.38	0.57	0.53	0.21	0.43
Syn	Med	1.00	0.81	1.42	1.27	0.79	0.80
Syn	Com	3.57	1.61	3.14	1.86	1.71	1.38
Sem	Sim	0.71	1.11	0.71	1.49	0.07	0.27
Sem	Med	0.57	1.13	0.71	1.50	0.00	0.00
Sem	Com	2.42	2.07	3.00	2.16	1.93	1.27

Note. [a]type of sentence condition; Syn = Syntactic condition; Sem = Semantic Condition
[b]Difficulty level; Sim = Simple; Med = Medium; Com = Complex

Table 5

Descriptive Statistics for Sentence Comprehension Errors on Second Administration

		PD On		PD Off	
Type[a]	Diff[b]	M	SD	M	SD
Syn	Sim	0.57	0.79	0.71	0.95
Syn	Med	1.42	1.98	1.42	1.27
Syn	Com	2.57	1.13	2.57	1.51
Sem	Sim	0.43	0.53	0.29	0.76
Sem	Med	0.71	0.95	0.85	1.07
Sem	Com	2.86	2.34	2.43	1.40

Note. [a]type of sentence condition; Syn = Syntactic condition; Sem = Semantic Condition
[b]Difficulty level; Sim = Simple; Med = Medium; Com = Complex

Due to the fact that that there was a 4-way interaction involving order, further analyses of sentence comprehension were performed only using each participants' first administration in order to examine the data without regard to order (e.g. the data of the seven subjects tested first on medication was compared with the data of the seven subjects tested off medication first). This

provided the most pure measure of the effect of medication without regard to the influence of repeated administrations. Analyses revealed an interaction between sentence difficulty and sentence structure $F(2, 11) = 8.99$, $p < .01$, with the syntactic sentences of medium difficulty being more difficult than the semantic sentences of medium difficulty. In addition, there was a main effect for sentence difficulty, $F(2, 11) = 18.2$, $p < .01$, with all three levels of difficulty being significantly different from each other for both groups.

In order to determine the impact order of administration may have played, analyses of sentence comprehension scores of participants' second administrations were also performed. Analyses revealed a main effect for sentence difficulty, $F(2, 11) = 27.86$, $p < .01$, with all three levels of difficulty being significantly different from each other for both medication conditions. The interaction between sentence difficulty and sentence structure was no longer significant. There were no medication main effects or interactions in either analysis (the first administration analysis or the second administration analysis) once order was removed.

To further evaluate the role medication played in the four-way interaction, separate comparisons were made of subjects in the on medication state and in the off medication state. Order was a between subjects factor, and sentence variables were within subjects factors. Analyses revealed a main effect of sentence difficulty for patients when on medication, $F(2, 11) = 22.83$, $p < .01$, and when off medication, $F(2, 11) = 22.44$, $p < .01$, with all three levels of difficulty being significantly different from each other. There were no interactions and no other main effects. Thus, medication did not play a role in the measurement of sentence comprehension.

None of the hypotheses for sentence comprehension concerning the effects of medication were supported, as there were no differences between patients on medication and off medication. The anticipated main effects and interactions for sentence structure and sentence difficulty were supported (syntactic sentences were generally more difficult than semantic sentences), suggesting manipulations of the sentences were effective in increasing difficulty.

With regard to the control group, comparisons were made between the control group and PD subjects both on and

off medication, as hypotheses have been proposed with regard to both comparisons.

T-tests revealed significant differences on the GDS between the control group (M = 5.00, SD = 3.78) and PD patients when on medication (M = 10.43, SD = 7.48), $t(26)$ = 2.61, p = .015, and the PD patients when off medication (M = 10.43, SD = 6.80), $t(26)$ = 2.42, p = .023. This supports the hypothesis predicting differences in depression between the control group and the PD group regardless of medication status. Due the impact that depression may have on cognition, analyses were conducted both with and without depression as a covariate where appropriate.

Scores on MMS were compared using two single factor (disease status) ANOVAs for both medication conditions compared to controls, with GDS as a covariate. Results revealed no significant differences between control MMS scores (M = 29.00, SD = 0.78) and the patients when on medication (M = 28.57, SD = 1.22) and the patients when off medication (M = 28.79, SD = 0.97), $Fs(2, 25)$ = 0.96 and 1.02, respectively, ps > .05. Analysis of the data without depression as a covariate yielded similar results.

The results on the word span task, the score on the BNT, and the score on the embedded figures task were

considered to be conceptually related in that they were all not expected to vary across disease status. Therefore they were analyzed using two single factor (disease status) MANOVAs for both medication conditions with and without GDS score as a covariate.

The control/PD off medication comparison of control tasks with GDS as a covariate revealed no significant main effect for disease status $F(3, 23) = 1.31$, $p = .295$. However, examination of univariate comparisons (still controlling for GDS scores) revealed a significant difference between control group scores on the BNT ($M = 27.64$, $SD = 2.06$) and the PD patients off medication ($M = 25.86$, $SD = 3.50$), $F(2, 25) = 5.20$, $p = .01$.

The control/PD off medication comparison of control tasks without GDS as a covariate revealed no significant main effect for disease status $F(3, 24) = 2.06$, $p = .132$. Examination of univariate comparisons did not reveal any significant differences between control group scores and the PD patients when off medication.

Similarly, the control/PD on medication comparison of control tasks (when controlling for GDS scores) revealed no significant main effect for disease status $F(3, 23) = 1.06$, $p = .386$. However, once again univariate comparisons (still controlling for GDS scores) revealed a

significant difference between control group scores on the BNT (M = 27.64, SD = 2.06) and the PD patients when on medication (M = 26.21, SD = 3.17), $F(2, 25) = 3.92$, p = .03.

The control/PD on medication comparison of control tasks without GDS as a covariate revealed no significant main effect for disease status $F(3, 24) = 1.62$, p = .210. Examination of univariate comparisons did not reveal any significant differences between control group scores and the PD patients when off medication.

These results are consistent with the proposed hypotheses which stated that as a group, these general measures of cognitive status would not differ between the control groups and the PD patients regardless of medication status. However, the univariate differences on the BNT were not expected.

The working memory task was analyzed with two 2 x 2 (task condition x disease status) ANCOVAs, with GDS as a covariate, for controls compared to subjects on medication, and subjects off medication. Examination of the comparison between controls and patients on medication revealed a main effect for task condition, $F(1, 25) = 7.77$, $p < .01$, with the phonologic task being significantly more difficult than the semantic task across

PD status, as the only significant effect. Examination of the comparison between controls and patients off medication revealed no significant main effects or interactions. Analysis of the data without depression as a covariate yielded similar results. These results did not support the hypothesis that controls would make fewer errors than PD subjects off medication.

The working memory task was also analyzed with one-tailed t-tests as specific hypotheses were proposed for the working memory task. Control patients performed significantly better than PD patients on medication on the semantic working memory task. There was not a significant difference between two groups on the phonologic working memory task (see table 6). There were no differences between controls and patients when off medication (see table 7). The difference between the patients when on medication and the control group was not expected.

Table 6

T-tests of # of Correct Responses on Working Memory and Sentence Comprehension Measures for PD Patients On Medication versus Controls

		PD On		Controls			
Variable	df	M	SD	M	SD	t	p*
WM Phon	26	11.6	4.32	12.0	3.33	0.25	.40
WM Sem	26	12.0	5.02	15.2	4.41	1.80	.04
Syntactic	26	31.7	2.31	33.3	1.86	2.44	.01
Semantic	26	32.1	3.40	34.0	1.36	1.90	.03

Note. PD On = Parkinson's patients on medication; WM Phon = phonological working memory task; WM Sem = semantic working memory task; Syntactic = syntactic sentence condition; Semantic = Semantic sentence condition; *p-values are one one-tailed

Table 7

T-tests of # of Correct Responses on Working Memory and Sentence Comprehension Measures for PD Patients Off Medication versus Controls

	PD Off			Controls			
Variable	df	M	SD	M	SD	t	p*
WM Phon	26	10.3	4.41	12.0	3.33	1.16	.13
WM Sem	26	12.8	5.49	15.2	4.41	1.29	.10
Syntactic	26	31.1	2.70	33.3	1.86	2.52	.01
Semantic	26	32.0	3.51	34.0	1.36	1.99	.03

Note. PD Off = Parkinson's patients off medication; WM Phon = phonological working memory task; WM Sem = semantic working memory task; Syntactic = syntactic sentence condition; Semantic = Semantic sentence condition; *p-values are one one-tailed

The sentence comprehension task was analyzed with 3 x 2 x 2 (sentence difficulty x sentence structure x disease status) ANOVAs, with GDS score as a covariate. Analysis of subjects off medication compared to control subjects revealed an interaction between GDS score and sentence difficulty $F(2, 24) = 4.61$, $p < .05$, with a main effect for sentence difficulty as well $F(2, 24) = 8.74$, $p < .01$. The main effect for disease status approached significance

$F(1, 25) = 3.20$, $p < .10$. Due to the interaction between the covariate and a factor (violating the assumption of homogeneity of regression slopes in ANCOVA), the data were re-analyzed substituting the GDS scores with (GDS scores - grand mean) in an effort to obtain a more accurate model, as well as explore the nature of the interaction. This analysis showed similar results. Examination of plots revealed that those subjects with lower levels of depression showed a greater increase in the number of errors between the medium and highest difficulty levels than those with higher levels of depression. These results did not support the hypotheses concerning PD patients' performance, but they did support hypotheses regarding sentence structure and complexity.

Analysis of sentence comprehension comparing subjects on medication to controls with GDS as a covariate yielded a three-way interaction (sentence structure x difficulty x GDS score), $F(2, 24) = 5.61$, $p < .01$. In addition there were two, two-factor interactions (sentence structure x difficulty; and difficulty x GDS score), $F(2, 24) = 11.34$, $p < .01$, and $F(2, 24) = 5.63$, $p < .01$, respectively. There was also a main effect for difficulty $F(2, 24) = 15.33$, $p < .01$. Once again, the data were reanalyzed substituting (GDS - grand mean) for GDS scores to obtain a

more accurate model for the data. This re-analysis showed similar results to prior analyses. Once again these results did not support hypotheses with regard to disease status, though differences with regard to sentence design were expected.

In an effort to examine the effect that depression was having on performance, the sentence comprehension task was re-analyzed without using GDS as a covariate. In an analysis comparing subjects off medication to controls, there was a main effect for PD status, $F(1, 26) = 6.05$, $p < .05$., with control subjects performing significantly better than PD subjects. In addition, there was an interaction between sentence construction and difficulty, $F(2, 25) = 7.13$, $p < .01$, with medium syntactic sentences being more difficult than medium semantic sentences. There were also main effects for sentence difficulty, $F(2, 25) = 49.90$, $p < .01$, and sentence structure, $F(1, 26) = 4.31$, $p < .05$, with syntactic sentences being more difficult than semantic sentences. These results were consistent with hypotheses.

In an analysis of sentence comprehension comparing subjects on medication to controls without covarying for depression, there was a main effect for PD status, $F(1, 26) = 6.03$, $p < .05$., with control subjects performing significantly better than PD subjects when on medication.

In addition, there was an interaction between sentence construction and difficulty, $F(2, 25) = 4.30$, $p < .05$, with syntactic difficulty increasing more rapidly than semantic difficulty. There was also a main effect for sentence difficulty, $F(2, 25) = 46.52$, $p < .01$, with each level of difficulty being significantly different from the other two. These results were consistent with hypotheses.

Analyses of the sentence comprehension data using one-tailed t-tests yielded similar results. Control subjects performed significantly better than PD patients when on medication on both semantic and syntactic sentences (see table 6). Control patients also performed significantly better than PD patients when off medication on both semantic and syntactic sentences (see table 7). These results were consistent with hypotheses.

Motor functioning may be used as a measure of dopamine levels in the brain, and as such may be correlated with cognitive functioning. Two-tailed post-hoc Pearson correlation analyses were performed examining the data for correlations between motor functioning as measured by the UPDR and those functions potentially sensitive to dopamine levels, e.g. working memory and sentence comprehension for medium and complex sentences. Significant correlations were found between the semantic

working memory task and motor functioning (see table 8) with higher levels of motor disability being associated with lower scores on the working memory task. There were no significant correlations between motor functioning and sentence comprehension.

Table 8

Correlations Between Working Memory Tasks and Motor Functioning as Measured by the UPDR

Task	UPDR On	UPDR Off
Sem Off	-.57*	-.72**
Sem On	-.53*	-.53*
Phon On	-.12	-.02
Phon Off	-.37	-.47

Note. Sem Off = semantic working memory task off medication; Sem On = semantic working memory task on medication; Phon On = phonological working memory task on medication; Phon Off = phonological working memory task off medication; * = $p < .05$; ** = $p < .01$.

Further two-tailed post-hoc Pearson correlation analyses were performed between the change in UPDR scores and the change in working memory scores to explore the relationship between changes in motor abilities and changes in working memory based on medication. There were

no significant correlations (see table 9). This provides further evidence that medication manipulation had an impact on motor functioning without a similar impact on working memory. Pearson correlation analyses between disease severity (as measured by UPDR score while on medication) and change in working memory scores also did not reach statistical significance.

Table 9

Correlations Between Difference Scores on Working Memory Tasks and Motor Functioning as Measured by the UPDR

Task	Sem Diff	Phon Diff	UPDR Diff
Sem Diff	--	-.05	-.32
Phon Diff	-.05	--	-.39
UPDR Diff	-.32	-.39	--

Note. Sem Diff = semantic working memory task on medication - semantic working memory task off medication; Phon Diff = phonological working memory task on medication - phonological working memory task off medication; UPDR Diff = UPDR score on medication - UPDR score off medication; * = $p < .05$; ** = $p < .01$.

DISCUSSION

This study examined working memory and sentence comprehension in Parkinson's disease in order to explore the role that basal ganglia may play in working memory and sentence comprehension. This was done by manipulating dopamine levels in individuals with Parkinson's disease. Participants with Parkinson's disease were also compared to participants without Parkinson's disease in order to contrast the effects of incipient parkinsonian dementia with deficits related to dopaminergic dysfunction. First the results of the control tasks and the depression measure will be discussed; next the effects of the medication manipulation and the impact dopamine deprivation may have had on basal ganglia functioning will be discussed; finally the relative performances of the PD patients and control subjects will be discussed.

Control Tasks and Depression

The hypotheses for the control tasks, as well as the hypotheses for levels of depression, were generally supported. There was no pattern of performance by the PD patients suggestive of a generalized cognitive decline, although there was some evidence of a deficit in confrontation naming. Findings in the literature with

regard to naming are not consistent. Other authors have found impairments in confrontation naming (Globus, Mildworf, & Melamed, 1985; Matison, Mayeux, Rosen & Fahn, 1982), though these findings are not universal (Cummings, Darkins, Mendez, Hill, & Benson, 1988; Pillon, Dubois, Lhermitte, & Agid, 1986). Although there are discrepancies in the literature regarding the specific nature of cognitive deficits in PD patients, there is a consensus that PD patients do not typically show a generalized cognitive decline across all cognitive domains (Bondi & Troster, 1997). The current results are in accord with this. The hypothesis for depression was supported as well, with PD patients being significantly more depressed than control subjects as measured by the GDS. This is in accord with the literature as well, which indicates that 40% of patients with PD experience significant depression (Cummings, 1992; Elwan et al., 1996).

Effects of Dopamine Manipulation

Despite the fact that measurement of motoric symptoms of PD indicated manipulation of dopamine levels was effective, there were no differences on any of the cognitive measures when participants were compared with dopamine at peak levels and when dopamine was at a reduced level. This did not support the hypotheses that performance on measures of working memory and sentence

comprehension would be dependent on intact basal ganglia functioning as measured by dopamine levels.

Prior research examining memory performance in PD patients on and off medication has yielded inconsistent results. The present study attempted to control potential contributors to variability shown in previous studies, including minimum criteria for duration of PD, controlling for the effect of coexisting dementia, and attempting to measure discrete aspects of working memory and sentence comprehension. There are at least two potential factors that influenced the results and obscured deficits that may have been otherwise attributable to dopamine deficits and striatal degeneration. The first relates to levels of dopamine. Despite the fact that motor scores changed as a result of medication manipulation, dopamine may not have been sufficiently reduced through manipulation of medication regimens to create cognitive deficits. Withholding medication for a longer period of time may have provided different results. Kulisevsky et al. (1996) reported plasma levodopa concentrations of virtually zero following a 12-hour withdrawal of oral levodopa, suggesting that additional delay would not reduce plasma dopamine levels significantly beyond what was obtained in the current study. However, significant concentrations of levodopa may remain in the brain beyond the 12-hour delay measured by Kulisevsky et al. (1996), as many PD patients do not become overtly parkinsonian for one or more days

off of medication. Thus additional length of medication withdrawal may indeed have further impact on cognition.

The second factor relates to disease duration. Patients may not have been far enough into the disease process to be experiencing a level of striatal dysfunction, particularly in the caudate, significant enough to cause measurable disruption of the cortico-striato-pallido-thalamo-cortical loops important for cognition. Despite the fact that dopamine depletion has been shown to occur in both the caudate and putamen, the greatest degenerative impact is centered in the putamen (Javoy-Agid & Agid, 1980; Jellinger, 1987; Kish et al., 1988; Lloyd et al., 1975). This has two implications.

First, as the cortical connections primarily arise from the caudate, it is possible that there may be demonstrable motor deficits due to dysfunction of the putamen, while caudate function remains relatively normal. Thus, even when patients are withdrawn from levodopa medication, cortical systems linked to the caudate may remain functionally intact.

Second, Kulisevsky et al. (1996) commented on the possibility that the levodopa doses required to remedy the dopamine deficits in the putamen may functionally "overdose" those structures where dopamine levels are relatively intact. Thus when patients are on doses of levodopa sufficient to compensate for motor deficits, cognition may be negatively impacted as structures

relevant for cognition become "overdosed." They suggested that the pharmacokinetic profile of patients may be the best predictor for cognitive deficits, with more advanced PD patients (as demonstrated through evidence of wearing off phenomena) showing increased sensitivity to changes in levodopa concentrations. In fact, Kulisevsky et al. (1996) found differences on a measure of frontal lobe functioning only after dividing their group based on "wearing off" phenomenon, with a group that did not show fluctuating motor deficits as drug levels were reduced, and a group that did show fluctuating motor deficits as drug levels decreased.

However, other investigators have suggested that the proposed "overdosing" of structures is not a valid explanation for varied cognitive performance in PD. Nadeau, Couch, Devane, & Shukla (1995) described basal ganglia structures with normal dopaminergic innervation as being able to buffer extracellular dopamine concentrations by taking up excess dopamine. Therefore a normal caudate will have normal interstitial dopamine concentrations regardless of how much dopamine is administered to an individual. In dopamine depleted structures, however, buffering capacity is lost, and very high dopamine concentrations can result from exogenous administration of L-dopa. In rats that have been lesioned with 6-hydroxydopamine, dopamine concentrations 200 times normal have been observed. This would suggest that it is

impossible to "overdose" basal ganglia structures, contradicting the hypotheses proposed by Kulisevsky et al. (1996).

In the present study, working memory was associated with decreased motor functioning, but the correlation was across medication status. More severe motor disturbances were associated with decreased performance on semantic working memory regardless of dopamine levels. This suggests that the deficits associated with semantic working memory are not related specifically to dopamine, but may rather be related to the general level of the disease. This is further supported by the fact that the PD patients performed significantly worse that control subjects on the semantic working memory task, suggesting that this deficit in semantic working memory may be related to an incipient parkinsonian dementia.

With regard to the underlying mechanisms influencing performance on the cognitive tasks, current results suggest that basal ganglia dysfunction, as influenced by dopamine disregulation, did not appear to play a critical role. Although several cautions (described above) are in order when discussing the dopamine manipulation, the virtually identical performance of patients on and off medication would suggest that dopaminergic deficits, hence basal ganglia dysfunction, were not primarily responsible for the differences between PD patients and controls seen on sentence comprehension and working memory. Comparison

with the control group indicated that the PD patients did show deficits in both sentence comprehension and semantic working memory providing further evidence that deficits in sentence comprehension and working memory are not related specifically to basal ganglia dysfunction and may instead be related to dysfunction in other brain systems. Additionally, working memory was not correlated with changes in motor functioning, further suggesting that basal ganglia dysfunction did not impact working memory. Other authors have also found behavioral (Cooper et al., 1992; Pillon, Dubois, Bonnet et al., 1989; Pillon, Dubois, Cusimano et al., 1992) and anatomical evidence (de la Monte et al., 1989) of degeneration of non-basal ganglia systems in patients with PD, including diffuse cortical degeneration, degeneration of the ascending cholinergic system from the nucleus of Meynert, and degeneration in the area of the amygdala.

Furthermore, the current results call into question the relationship of the caudate to the prefrontal cortex in relation to cognition. The functional implications of the "dorsolateral prefrontal" circuit described by Alexander et al. (1990) were significantly less developed than those of the "motor" circuit (e.g. motoric deficits following disruption of this circuit are directly observable, while cognitive changes are more difficult to measure). Even with the relative ease of measuring motor output as contrasted to cognitive output, there are still

significant questions about the exact nature of the motor pathways including the interaction of the "direct" and "indirect" pathways. These questions are amplified by the difficulty inherent in observing cognitive processing. The current study may not tap discrete enough aspects of the dorsolateral-prefrontal circuit, and as such may not be sensitive to breakdown of the circuit. A second possibility is that higher order cortical processing may not be impacted by basal ganglia dysfunction, suggesting that basal ganglia structures are not central to processing of information.

There may also have been task-specific factors that affected the results. As described in the introduction, relatively few studies have examined the relationship between dopamine and cognition, and results of those studies have been mixed. These varying results are likely due to a number of factors. One factor specific to the working memory task used in the current study may relate to the concept of internally versus externally controlled processing, as basal ganglia structures may have different importance depending on the nature of the task. Some authors have proposed that PD patients may have deficits on tasks requiring internal generation of encoding, retrieval, and problem-solving strategies (Buytenhuijs et al., 1994; Dubois & Pillon, 1997; Van Spaendonck, Berger, Horstink, Borm, & Cools, 1996), while tasks with external requirements are relatively intact. Spaendonck et al.

(1996) found that PD patients profited from cues only when they were explicit (patients are provided guidelines for memorization through cues), and not when cues were implicit (i.e. patients were required to create a strategy to take advantage of the cues). Despite the fact that the current task had both semantic and phonologic components, the cues for both conditions were explicit. The patients had information about whether they should adopt a semantic or phonological framework, as well as about the type of cue they would receive. When interpreted in the context of the internal/external processing paradigm, the current task may be seen as being more heavily loaded on the external side of the equation, and this may have been a factor in the current results.

A second factor contributing to mixed findings in the literature may be variations in "simultaneous" processing. For example, Malapani et al. (1994) found dopamine related deficits when PD patients were required to attend to two cues simultaneously and provide two responses simultaneously as well. In the current study, subjects were asked to attend to a list, attend to counting, and then attend to the original list. In one sense, the subjects were performing a sequential task in the current study. Although information was overlapping, subjects were only asked to attend to one piece of information at a time. Thus, deficits in simultaneous task performance may not have been adequately tapped in the current study.

Studies comparing PD patients' memory on and off medication have generally focused on delayed memory. Those studies have inconsistent results with some finding no memory differences related to medication status (Gotham et al., 1988; Kulisevsky et al., 1996; Lange et al., 1992; Pillon et al., 1989), and others finding differences (Gabrieli et al., 1996; Mohr et al., 1987). Those studies that did attempt to examine verbal working memory specifically, tended to use the Brown-Peterson paradigm, in which subjects must remember a series of three letters over a delay period while counting backward. In some respects, the Brown-Peterson paradigm is similar to the current task, however, there is no cueing involved in that paradigm. This difference in cueing may have been an important factor in the non-significant results in the current study, as evidence suggests PD patients benefit from cueing (Crosson, 1992; Dubois & Pillon, 1997; Faglioni et al., 1995, 1997).

With regard to sentence comprehension, it was found that sentence comprehension was not related to dopamine status as PD groups performed virtually identically when tested with dopamine at peak levels or with dopamine at diminished levels on the sentence comprehension task. It was hypothesized that there would be differences between the PD patients off medication, the PD the PD patients on medication, and the control group on both the working memory tasks and the sentence comprehension tasks. The

current results suggest that sentence comprehension deficits seen in PD patients are independent of basal ganglia dysfunction. The relationship between sentence comprehension and working memory in PD patients and control subjects will be discussed in the following section.

Comparison of PD Patients with Control Subjects

With regard to the working memory task created for this project, the only hypothesis supported was the difference on the semantic working memory task between the PD patients on medication and control subjects. There were no differences between the PD groups when compared on and off medication, and there were no differences between either of the PD groups and the control group on the phonological working memory task.

These results for working memory are not consistent with a number of studies that have found more robust differences on measures of verbal working memory between PD patients and control subjects (Cooper & Sagar, 1993; Cooper, Sagar, & Sullivan, 1993; Dalrymple-Alford et al., 1994; Gabrieli, Singh, Stebbins, & Goetz, 1996; Sullivan et al., 1993). This is mildly surprising in that each of these studies employed techniques to measure working memory that were largely similar to the present study. Each of the studies cited above employed verbal memory task requiring recall of some sort of list (e.g. number, letters, or words) across a distraction task. However,

the working memory portion in each of the above studies involved free recall. In the current study, the recall portion was cued (e.g. "A type of animal" or "rhymes with dog"). The cues were used in the design in an effort to bias encoding to examine both semantic and phonologic working memory. However, these cues may have been a fundamental distinction between the current design and other cited studies, and disguised retrieval deficits in the PD patients. This effect would be consistent with literature stating that PD patients tend to have retrieval deficits (Crosson, 1992; Dubois & Pillon, 1997; Faglioni et al., 1995, 1997). Thus the deficits cited in the previous studies of working memory in PD patients may be related to retrieval deficits, while the lack of deficits in the current study may have been related, in part, to the use of a cueing procedure.

There were only minimal differences on the working memory measures suggesting that the differences in sentence comprehension deficits found between PD patients and controls may be in part due to deficits in working memory, but likely reflect additional deficits in other areas such as syntax. Researchers have found impairment in sentence comprehension in PD patients, and those results are not inconsistent with those obtained in the current study (Grossman et al., 1993, 1992, 1991). The pattern of performance of PD patients in the current study was comparable to cited literature, as PD patients had

significantly more difficulty on more complicated sentences than on simpler sentences, though there were no 3-way interactions between sentence structure, difficulty, and PD status. The deficits seen in the cited studies were theorized to be multifactorial in nature, including both grammatical and attentional components. This hypothesis is consistent with the current study, although the present study implicates working memory as an additional factor contributing to comprehension deficits, and minimizes the attentional component as attentional deficits would have been expected to cause deficits in a number of measures. The impact of deficient working memory is further supported by the fact that there were differences between controls and PD patients on the semantic sentences which involved minimal syntactic processing.

Martin (1993) suggests that sentence processing and working memory measured through word span are dissociable. The present study supports this proposal, in that there were consistent deficits in sentence comprehension across medication condition with only variable deficits in phonological or semantic working memory. Martin (1993) proposed that there may be a separate role for syntactic processing relying on syntactic working memory involved in sentence processing. The present study does not address the question of syntactic working memory directly, but it does suggest that there are elements beyond phonological

and semantic working memory impacting the performance of PD patients on sentence comprehension.

The current study also raises the possibility that depression (and the impact it may have on cognition) is an additional factor that affects performance. Due to the fact that depression may impact cognition (Kuzis, Sabe, Tiberti, Leiguarda, & Starkstein, 1997; Starkstein, Bolduc, Mayberg, Preziosi & Robinson, 1990; Troster, Paolo, et al., 1995; Troster, Stalp, et al., 1995), and the PD groups were both experiencing significantly greater levels of depression than the control group, depression cannot be ruled out as a factor that lead to deficits. Depression was not measured in any of the Grossman et al. (1991, 1992, 1993) studies, and this may be an important factor, particularly when deficits are proposed to be multifactorial in nature, and depression occurs in approximately 40% of patients with PD (Cummings, 1992; Elwan et al., 1996). However, it is possible that PD both causes depression and impacts sentence processing, but that depression is not responsible for the changes in sentence processing. This may be evaluated more directly in future studies through the use of an age and education matched control group that is also matched on level of depression.

Future Research

The relatively robust lack of a medication effect in the current study offers several possibilities to further

define the scope of the basal ganglia in working memory. The first possibility is to increase the length of time patients are withdrawn from medication to insure that dopamine levels in the brain are minimized. This may be necessary to insure that the current results were not simply due to insufficient dopamine withdrawal.

A second possibility relates to the measurement of working memory and simultaneous processing. A relatively simple task requiring true simultaneous processing, such as used in the Malapani et al. (1994), could be administered on and off medication, and would be expected to show dopamine related deficits. A working memory measure could also be administered, and if changes were not found based on medication it would suggest that deficits in attentional resources, but not working memory, are related to basal ganglia dysfunction.

A third possibility is to explore the differences between internally and externally mediated tasks, and the relationship that this dimension has to basal ganglia functioning. Working memory may be tapped using either type of task, and if the two types of tasks were dissociable, it would suggest that working memory is not specifically affected by basal ganglia dysfunction. Specifically, it may be interesting to have patients perform a task with little guidance initially, followed by performing the same task a second time with explicit instructions, and see if PD patients improve significantly

more than healthy controls across conditions. Alternatively, the performances of individuals with varying levels of dopamine could be compared in a similar paradigm. The current working memory task may be altered by not providing subjects with the type of cue that will follow each list, and/or mixing semantic and phonological cues for each list.

With regard to the sentence comprehension measures, the current study argues against global deficits in attention or memory as being primarily responsible for deficiencies in sentence comprehension, as a variety of measures showed no differences between PD patients and controls. Further research may center around defining the nature of syntactic memory and processing, and what, if any, relationship this has to the basal ganglia. Although difficult to conceptualize, development of measures to assess syntactic functioning may provide information about the nature of language deficits in individuals with basal ganglia dysfunction.

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APPENDIX
EXPERIMENTAL TEST PROTOCOLS

Name/ID Number:_____

Date:_____

Length of Longest List with at Least 50% Correct_____

Word Span

Instructions for Examiner: Give before working memory tasks to determine word span. Present items at a rate of 1 per second. For each level, give 2 trials. The first time the subject misses a trial, continue giving trials at the same level until the subject gets at least 2 right; then, proceed to the next level. A trial is passed only if items and order are both correct. Span is defined as the last level at which the subject gets at least 2 trials correct. If the subject does not miss more than 50% up to and including the 7-word level, span is defined as 7.

Instructions to Subject: **I am going to say a short list of words. When I am through, I want you to repeat the words I said in the same order as I said them.**

Right Wrong

3 words

_____ _____ frown, bolt, kettle

_____ _____ vase, cake, pocket

_____ _____ highway, nest, river

_____ _____ water, lens, dust

4 words

_____ _____ gift, quart, zipper, meat

_____ _____ wood, school, thread, jar

_____ _____ glass, letter, berry, queen

_____ _____ village, hook, card, moss

Bruce Crosson & Reid Skeel, March 17, 1994

Right Wrong

5 words

____ ____ basket, road, wife, gate, king

____ ____ book, vein, puddle, dinner, juice

____ ____ team, night, cement, yard, horn

____ ____ root, metal, quill, weed, dime

6 words

____ ____ tunnel, liver, cube, gutter, pole, wreck

____ ____ bell, kiss, quilt, forest, velvet, dome

____ ____ flower, jet, whisker, rail, mile, helmet

____ ____ pepper, haze, crow, nurse, sugar, yellow

7 words

____ ____ woman, parade, town, zoo, kite, face, blood

____ ____ doctor, twig, lumber, gun, purse, bath, jewel

____ ____ rock, tennis, money, pipe, white, cream, hostage

____ ____ land, wall, napkin, rain, silk, dawn, grass

Rhyme Recognition

Instructions for Examiner: Give the subject the following instructions. Embellish as necessary to facilitate comprehension of the task. Give before working memory tasks to establish subjects' ability to recognize rhyme.

Instructions to Subject: **I am going to say 2 words. Then I will say, "rhymes with . . .", and I will say 1 more word. This last word will rhyme with one of the first 2 words. I want you to say which of the 2 words rhymes with the last word I give you. For example, I might say "frost - lime", and then I would say, "rhymes with time". You would respond . . . (Let subject answer. If he/she is correct say, "good". If incorrect, say, "That's not quite correct, lime rhymes with time." Then, give the following additional sample, "hand - cheese; rhymes with brand"). Now let's do some more.**

1. pump - black

   rhymes with stack

2. tray - door

   rhymes with play

3. cave - sky

   rhymes with brave

4. fence - spool

   rhymes with tool

5. mast - beard

   rhymes with last

6. rash - child

   rhymes with wild

7. coin - tar

   rhymes with car

8. date - toast

   rhymes with late

10. beef - trip

    rhymes with slip

11. pill - game

    rhymes with tame

12. pearl - hawk

    rhymes with girl

Category Recognition

Instructions for Examiner: Give the subject the following instructions. Embellish as necessary to help them understand the task. Give this task before the working memory tasks to establish their ability to recognize categorization.

Instructions to Subject: **I am going to say 2 words. Then, I will give you a category, and one of the words will fit into that category. I want you to tell me which word fits into the category. For example, I might say, "tiger - boat"; then I would say, "a kind of cat". You would say . . . (Allow subject to respond. If they say "tiger", say "good". If not, say, "That's not quite correct. A tiger is a kind of cat." Then, give them the following additional sample, "carpet - rose; a kind of flower".) Now let's do some more.**

1. biscuit - shower

   something to eat

2. dial - tennis

   a sport

3. flannel - rope

   a kind of cloth

4. chain - milk

   something to drink

5. hamster - brick

   a pet

6. garden - spear

   a weapon

7. candy - sparrow

   a bird

8. palm - curb

   a tree

9. tractor - gold

   a metal

10. library - wheat

    a public building

11. miner - cloud

    a kind of work

12. lock - storm

    a kind of weather

Name/ID Number:_____ Number of words recalled:_____

Date:_____ Number of correct monitoring responses:_____

Number of words per list:_____

RHYMING WORD LIST

Form A

Instructions for Examiner: Give the subject the following instructions. Embellish as necessary to help them understand the task.

When administering the word list, present words at a rate of 1 per second. Present the target number quickly after the last word in the list; i.e. leave as small a pause as possible between the last word and the target number. This is done to prevent (or at least to minimize) maintenance rehearsal. If you notice a subject rehearsing the word list before beginning to count backwards, instruct them not to do so. Subjects are to count backward from the target number by increments of three for 9 seconds prior to being given the stimulus cue. If subjects do not respond encourage them once to guess, even if they claim to have no recollection. Be sure to record all responses. Even if the subjects correct themselves, be sure to write the first response as well as subsequent responses.

Record Keeping: Place a check mark next to every word on the list for which the subject raises their finger.

Instructions to Subject: **I am going to read a list of words. While I'm reading the list, I want you to raise your finger everytime you hear a word with the letter "B" in it. So if I said "Sky, bone, spool," you would lift your finger when I said bone.**

After I finish reading the list, I'll say a number, and I want you to start counting backward by two's from that number. So I would say, "sky, bone, spool, 60," and you would start counting backward (allow subject to count backwards for a few seconds).

Then I will give you some hints about the sounds of words from the list that I want you to remember.

For example, I might say "sky, bone, spool, 60." You would raise your finger as I say bone. Then you would start counting backward by two from 60 out loud (allow subject to start counting for a few seconds), then, if I said "rhymes with pie", you would say . . . (Allow subject to respond. If they say "sky," say "good." If not, say that's not quite correct, sky was the word on the list which rhymed with pie.) Give next sample even if this one was done successfully.

Let's try another, "coin, bait, clip, 90" (After a few seconds, say "rhymes with slip.")

Let's do one more. "chain, bolt, foil, 127." Rhymes with toil.

Now we are ready to start. Again, I will read you a list of words and you should listen for words with the letter "B" in them. Then I will give you a number. Count backwards by two as soon as I give you the number. After you have been counting for a while, I will give you some hints about the sound of words on the list that I want you to remember. Ready, let's begin.

Rhyming Word List A
Page: 2

List 1

1) fox	1) fox	1) fox	1) fox	1) fox
2) lime	2) lime	2) card	2) card	2) card
3) knife	3) card	3) lime	3) lime	3) moon
	4) knife	4) moon	4) moon	4) lime
		5) knife	5) train	5) train
			6) knife	6) door
				7) knife

Starting number: 89

_____ **1) rhymes with box (fox)**
_____ **2) rhymes with time (lime)**
_____ **3) rhymes with life (knife)**

List 2

1) flea	1) flea	1) flea	1) flea	1) flea
2) nose	2) cake	2) cake	2) cake	2) cake
3) boat	3) nose	3) nose	3) chair	3) chair
	4) boat	4) chair	4) nose	4) nose
		5) boat	5) iron	5) iron
			6) boat	6) purse
				7) boat

Starting number: 105

_____ **1) rhymes with moat (boat)**
_____ **2) rhymes with see (flea)**
_____ **3) rhymes with hose (nose)**

List 3

1) sock	1) sock	1) sock	1) sock	1) sock
2) frog	2) toast	2) toast	2) toast	2) toast
3) drill	3) frog	3) frog	3) bank	3) bank
	4) drill	4) bank	4) frog	4) frog
		5) drill	5) crown	5) crown
			6) drill	6) stain
				7) drill

Starting number: 92

_____ **1) rhymes with log (frog)**
_____ **2) rhymes with lock (sock)**
_____ **3) rhymes with fill (drill)**

Rhyming Word List A
Page: 3

List 4

1) bean	1) bean	1) bean	1) bean	1) bean
2) face	2) face	2) cannon	2) cannon	2) cannon
3) lice	3) cannon	3) face	3) face	3) tire
	4) lice	4) tire	4) tire	4) face
		5) lice	5) dust	5) dust
			6) lice	6) stone
				7) lice

Starting number: 45

_____ 1) rhymes with lean (bean)
_____ 2) rhymes with mice (lice)
_____ 3) rhymes with space (face)

List 5

1) fan	1) fan	1) fan	1) fan	1) fan
2) boot	2) bed	2) bed	2) bed	2) bed
3) mouse	3) boot	3) boot	3) sack	3) sack
	4) mouse	4) sack	4) boot	4) boot
		5) mouse	5) lake	5) lake
			6) mouse	6) vase
				7) mouse

Starting number: 123

_____ 1) rhymes with house (mouse)
_____ 2) rhymes with loot (boot)
_____ 3) rhymes with man (fan)

List 6

1) mug	1) mug	1) mug	1) mug	1) mug
2) head	2) head	2) peanut	2) peanut	2) peanut
3) gown	3) peanut	3) head	3) head	3) coal
	4) gown	4) coal	4) coal	4) head
		5) gown	5) yard	5) yard
			6) gown	6) sword
				7) gown

Starting number: 75

_____ 1) rhymes with dead (head)
_____ 2) rhymes with clown (gown)
_____ 3) rhymes with bug (mug)

Reid Skeel & Bruce Crosson, June 2, 1994

Rhyming Word List A
Page: 4

List 7

1) crow	1) crow	1) crow	1) crow	1) crow
2) plum	2) plum	2) dust	2) brick	2) brick
3) doll	3) brick	3) plum	3) plum	3) dust
	4) doll	4) brick	4) dust	4) plum
		5) doll	5) hook	5) hook
			6) doll	6) seat
				7) doll

Starting number: 131

_____ **1) rhymes with slow** (crow)
_____ **2) rhymes with drum** (plum)
_____ **3) rhymes with mall** (doll)

List 8

1) trout	1) trout	1) trout	1) trout	1) trout
2) coat	2) bomb	2) bomb	2) bomb	2) bomb
3) lamp	3) coat	3) coat	3) doctor	3) doctor
	4) lamp	4) doctor	4) coat	4) coat
		5) lamp	5) farm	5) farm
			6) lamp	6) park
				7) lamp

Starting number: 63
_____ **1) rhymes with shout** (trout)
_____ **2) rhymes with camp** (lamp)
_____ **3) rhymes with float** (coat)

List 9

1) plate	1) plate	1) plate	1) plate	1) plate
2) snake	2) snake	2) book	2) book	2) book
3) beet	3) book	3) snake	3) snake	3) mint
	4) beet	4) mint	4) mint	4) snake
		5) beet	5) nest	5) nest
			6) beet	6) gutter
				7) beet

Starting number: 101

_____ **1) rhymes with meat** (beet)
_____ **2) rhymes with lake** (snake)
_____ **3) rhymes with grate** (plate)

Rhyming Word List A
Page: 5

List 10

1) jaw	1) jaw	1) jaw	1) jaw	1) jaw
2) pants	2) rice	2) rice	2) rice	2) rice
3) shark	3) pants	3) pants	3) wallet	3) wallet
	4) shark	4) wallet	4) pants	4) pants
		5) shark	5) tack	5) tack
			6) shark	6) grass
				7) shark

Starting number: 51

_____ **1) rhymes with chants** (pants)
_____ **2) rhymes with mark** (shark)
_____ **3) rhymes with law** (jaw)

Name/ID Number:_____

Number of words recalled:_____

Date:_____

Number of correct monitoring responses:_____

Number of words per list:_____

RHYMING WORD LIST

Form B

Instructions for Examiner: Give the subject the following instructions. Embellish as necessary to help them understand the task.

When administering the word list, present words at a rate of 1 per second. Present the target number quickly after the last word in the list; i.e. leave as small a pause as possible between the last word and the target number. This is done to prevent (or at least to minimize) maintenance rehearsal. If you notice a subject rehearsing the word list before beginning to count backwards, instruct them not to do so. Subjects are to count backward from the target number by increments of three for 9 seconds prior to being given the stimulus cue. If subjects do not respond encourage them once to guess, even if they claim to have no recollection. Be sure to record all responses. Even if the subjects correct themselves, be sure to write the first response as well as subsequent responses.

Record Keeping: Place a check mark next to every word on the list for which the subject raises their finger.

Instructions to Subject: I am going to read a list of words. While I'm reading the list, I want you to raise your finger everytime you hear a word with the letter "B" in it. So if I said "Sky, bone, spool," you would lift your finger when I said bone.

After I finish reading the list, I'll say a number, and I want you to start counting backward by two's from that number. So I would say, "sky, bone, spool, 60," and you would start counting backward (allow subject to count backwards for a few seconds).

Then I will give you some hints about the sounds of words from the list that I want you to remember.

For example, I might say "sky, bone, spool, 60." You would raise your finger as I say bone. Then you would start counting backward by two from 60 out loud (allow subject to start counting for a few seconds), then, if I said "rhymes with pie", you would say . . . (Allow subject to respond. If they say "sky," say "good." If not, say that's not quite correct, sky was the word on the list which rhymed with pie.) Give next sample even if this one was done successfully.

Let's try another, "coin, bait, clip, 90" (After a few seconds, say "rhymes with slip.")

Let's do one more. "chain, brick, foil, 127." Rhymes with toil.

Now we are ready to start. Again, I will read you a list of words and you should listen for words with the letter "B" in them. Then I will give you a number. Count backwards by two as soon as I give you the number. After you have been counting for a while, I will give you some hints about the sound of words on the list that I want you to remember. Ready, let's begin.

Rhyming Word List B
Page: 2

List 1

1) vest	1) vest	1) vest	1) vest	1) vest
2) toe	2) toe	2) blade	2) blade	2) blade
3) grape	3) blade	3) toe	3) toe	3) cloud
	4) grape	4) cloud	4) cloud	4) toe
		5) grape	5) lever	5) lever
			6) grape	6) mile
				7) grape

Starting number: 91

_____ 1) rhymes with blow (toe)
_____ 2) rhymes with best (vest)
_____ 3) rhymes with drape (grape)

List 2

1) cow	1) cow	1) cow	1) cow	1) cow
2) couch	2) sugar	2) sugar	2) sugar	2) sugar
3) pan	3) couch	3) couch	3) soup	3) soup
	4) pan	4) soup	4) couch	4) couch
		5) pan	5) army	5) army
			6) pan	6) thief
				7) pan

Starting number: 170

_____ 1) rhymes with can (pan)
_____ 2) rhymes with slouch (couch)
_____ 3) rhymes with now (cow)

List 3

1) belt	1) belt	1) belt	1) belt	1) belt
2) hand	2) bacon	2) bacon	2) bacon	2) bacon
3) gnat	3) hand	3) hand	3) straw	3) straw
	4) gnat	4) straw	4) hand	4) hand
		5) gnat	5) piano	5) piano
			6) gnat	6) rain
				7) gnat

Starting number: 135

_____ 1) rhymes with felt (belt)
_____ 2) rhymes with fat (gnat)
_____ 3) rhymes with land (hand)

Reid Skeel & Bruce Crosson, June 2, 1994

Rhyming Word List B
Page: 3

List 4

1) pea	1) pea	1) pea	1) pea	1) pea
2) deer	2) deer	2) bread	2) bread	2) bread
3) hoe	3) bread	3) deer	3) deer	3) mast
	4) hoe	4) mast	4) mast	4) deer
		5) hoe	5) wall	5) wall
			6) hoe	6) tunnel
				7) hoe

Starting number: 49

_____ **1) rhymes with sea** (pea)
_____ **2) rhymes with fear** (deer)
_____ **3) rhymes with flow** (hoe)

List 5

1) spoon	1) spoon	1) spoon	1) spoon	1) spoon
2) bee	2) box	2) box	2) box	2) box
3) shoe	3) bee	3) bee	3) bath	3) bath
	4) shoe	4) bath	4) bee	4) bee
		5) shoe	5) rifle	5) rifle
			6) shoe	6) rose
				7) shoe

Starting number: 86

_____ **1) rhymes with flue** (shoe)
_____ **2) rhymes with moon** (spoon)
_____ **3) rhymes with fee** (bee)

List 6

1) cat	1) cat	1) cat	1) cat	1) cat
2) peach	2) peach	2) paper	2) paper	2) paper
3) lung	3) paper	3) peach	3) peach	3) spear
	4) lung	4) spear	4) spear	4) peach
		5) lung	5) wax	5) wax
			6) lung	6) string
				7) lung

Starting number: 162

_____ **1) rhymes with beach** (peach)
_____ **2) rhymes with mat** (cat)
_____ **3) rhymes with rung** (lung)

Rhyming Word List B
Page: 4

List 7

1) bark	1) bark	1) bark	1) bark	1) bark
2) suit	2) suit	2) leg	2) leg	2) leg
3) stool	3) leg	3) suit	3) suit	3) dime
	4) stool	4) dime	4) dime	4) suit
		5) stool	5) paste	5) paste
			6) stool	6) net
				7) stool

Starting number: 101

_____ **1) rhymes with loot** (suit)
_____ **2) rhymes with fool** (stool)
_____ **3) rhymes with lark** (bark)

List 8

1) goat	1) goat	1) goat	1) goat	1) goat
2) pot	2) candy	2) candy	2) candy	2) candy
3) ball	3) pot	3) pot	3) cigar	3) cigar
	4) ball	4) cigar	4) pot	4) pot
		5) ball	5) mat	5) mat
			6) ball	6) sack
				7) ball

Starting number: 72

_____ **1) rhymes with moat** (goat)
_____ **2) rhymes with call** (ball)
_____ **3) rhymes with cot** (pot)

List 9

1) rake	1) rake	1) rake	1) rake	1) rake
2) corn	2) corn	2) trash	2) trash	2) trash
3) fly	3) trash	3) corn	3) corn	3) corn
	4) fly	4) land	4) land	4) land
		5) fly	5) ring	5) ring
			6) fly	6) hall
				7) fly

Starting number: 136

_____ **1) rhymes with flake** (rake)
_____ **2) rhymes with horn** (corn)
_____ **3) rhymes with dry** (fly)

Rhyming Word List B
Page: 5

List 10

1) hat	1) hat	1) hat	1) hat	1) hat
2) feet	2) tent	2) tent	2) tent	2) tent
3) dog	3) feet	3) feet	3) cave	3) cave
	4) dog	4) cave	4) feet	4) feet
		5) dog	5) tank	5) tank
			6) dog	6) wire
				7) dog

Starting number: 48

_____ **1) rhymes with log** (dog)
_____ **2) rhymes with flat** (hat)
_____ **3) rhymes with sleet** (feet)

Name/ID Number:_____ Number of words recalled:_____

Date:_____ Number of correct monitoring responses:_____

Number of words per list:_____

SEMANTIC WORD LIST

Form A

Instructions for Examiner: Give the subject the following instructions. Embellish as necessary to help them understand the task.

When administering the word list, present words at a rate of 1 per second. Present the target number quickly after the last word in the list; i.e. leave as small a pause as possible between the last word and the target number. This is done to prevent (or at least to minimize) maintenance rehearsal. If you notice a subject rehearsing the word list before beginning to count backwards, instruct them not to do so. Subjects are to count backward from the target number by increments of two for 9 seconds prior to being given the stimulus cue. If subjects do not respond encourage them once to guess, even if they claim to have no recollection. Be sure to record all responses. Even if the subjects correct themselves, be sure to write the first response as well as subsequent responses.

Record Keeping: Place a check mark next to every word on the list for which the subject raises their finger.

Instructions to Subject: **I am going to read a list of words. While I'm reading the list, I want you to raise your finger everytime you hear something that is edible. So if I said "flannel, biscuit, tennis, you would lift your finger when I said biscuit.**

After I finish reading the list, I'll say a number, and I want you to start counting backward by two's from that number. So I would say flannel, biscuit, tennis, 60" and you would start counting backward (allow subjects to count backwards for a few seconds).

Then I will give you some hints about the meaning of words on the list that I want you to remember.

For example, I might say "flannel, biscuit, tennis, 60." You would raise your finger as I say biscuit. Then you would start counting backward by two from 60 out loud (allow subject to start counting for a few seconds), then, if I said "a sport", you would say . . . (Allow subject to respond. If they say "tennis," say "good." If not, say that's not quite correct, tennis was the word on the list which was a sport.) Give next sample even if this one was done successfully.

Let's try another, "milk, hamster, spear, 90" (After a few seconds, say "a type of liquid.")

Let's do one more. "Gold, curb, sparrow, 90." A type of metal.

Now we are ready to start. Again, I will read you a list of words and you should listen for things that are edible. Then I will give you a number. Count backwards by two as soon as I give you the number. After you have been counting for a while, I will give you some hints about sounds of words on the list I want you to remember. Ready, let's begin.

Semantic Word List A
Page: 2

List 1

1) fox	1) fox	1) fox	1) fox	1) fox
2) lime	2) lime	2) card	2) card	2) card
3) knife	3) card	3) lime	3) lime	3) moon
	4) knife	4) moon	4) moon	4) lime
		5) knife	5) train	5) train
			6) knife	6) door
				7) knife

Starting number: 45

_____ 1) an animal (fox)
_____ 2) a fruit (lime)
_____ 3) something from a kitchen (knife)

List 2

1) flea	1) flea	1) flea	1) flea	1) flea
2) nose	2) cake	2) cake	2) cake	2) cake
3) boat	3) nose	3) nose	3) chair	3) chair
	4) boat	4) chair	4) nose	4) nose
		5) boat	5) iron	5) iron
			6) boat	6) purse
				7) boat

Starting number: 180

_____ 1) a means of transportation (boat)
_____ 2) an insect (flea)
_____ 3) part of the body (nose)

List 3

1) sock	1) sock	1) sock	1) sock	1) sock
2) frog	2) toast	2) toast	2) toast	2) toast
3) drill	3) frog	3) frog	3) bank	3) bank
	4) drill	4) bank	4) frog	4) frog
		5) drill	5) crown	5) crown
			6) drill	6) stain
				7) drill

Starting number: 97

_____ 1) an animal (frog)
_____ 2) an article of clothing (sock)
_____ 3) a tool (drill)

Semantic Word List A
Page: 3

List 4

1) bean	1) bean	1) bean	1) bean	1) bean
2) face	2) face	2) cannon	2) cannon	2) cannon
3) lice	3) cannon	3) face	3) face	3) tire
	4) lice	4) tire	4) tire	4) face
		5) lice	5) dust	5) dust
			6) lice	6) stone
				7) lice

Starting number: 132

_____ **1) a vegetable** (bean)
_____ **2) type of insects** (lice)
_____ **3) a part of the body** (face)

List 5

1) fan	1) fan	1) fan	1) fan	1) fan
2) boot	2) bed	2) bed	2) bed	2) bed
3) mouse	3) boot	3) boot	3) sack	3) sack
	4) mouse	4) sack	4) boot	4) boot
		5) mouse	5) lake	5) lake
			6) mouse	6) vase
				7) mouse

Starting number: 52

_____ **1) an animal** (mouse)
_____ **2) an article of clothing** (boot)
_____ **3) a household appliance** (fan)

List 6

1) mug	1) mug	1) mug	1) mug	1) mug
2) head	2) head	2) peanut	2) peanut	2) peanut
3) gown	3) peanut	3) head	3) head	3) coal
	4) gown	4) coal	4) coal	4) head
		5) gown	5) yard	5) yard
			6) gown	6) sword
				7) gown

Starting number: 155

_____ **1) a part of the body** (head)
_____ **2) an article of clothing** (gown)
_____ **3) something from a kitchen** (mug)

Semantic Word List A
Page: 4

List 7

1) crow	1) crow	1) crow	1) crow	1) crow
2) plum	2) plum	2) dust	2) brick	2) brick
3) doll	3) brick	3) plum	3) plum	3) dust
	4) doll	4) brick	4) dust	4) plum
		5) doll	5) hook	5) hook
			6) doll	6) seat
				7) doll

Starting number: 83

_____ **1) an animal** (crow)
_____ **2) a fruit** (plum)
_____ **3) a toy** (doll)

List 8

1) trout	1) trout	1) trout	1) trout	1) trout
2) coat	2) bomb	2) bomb	2) bomb	2) bomb
3) lamp	3) coat	3) coat	3) doctor	3) doctor
	4) lamp	4) doctor	4) coat	4) coat
		5) lamp	5) farm	5) farm
			6) lamp	6) park
				7) lamp

Starting number: 114

_____ **1) a type of fish** (trout)
_____ **2) a piece of furniture** (lamp)
_____ **3) an article of clothing** (coat)

List 9

1) plate	1) plate	1) plate	1) plate	1) plate
2) snake	2) snake	2) book	2) book	2) book
3) beet	3) book	3) snake	3) snake	3) mint
	4) beet	4) mint	4) mint	4) snake
		5) beet	5) nest	5) nest
			6) beet	6) gutter
				7) beet

Starting number: 190

_____ **1) a vegetable** (beet)
_____ **2) an animal** (snake)
_____ **3) something from a kitchen** (plate)

Semantic Word List A
Page: 5

List 10

1) jaw	1) jaw	1) jaw	1) jaw	1) jaw
2) pants	2) rice	2) rice	2) rice	2) rice
3) shark	3) pants	3) pants	3) wallet	3) wallet
	4) shark	4) wallet	4) pants	4) pants
		5) shark	5) tack	5) tack
			6) shark	6) grass
				7) shark

Starting number: 41

_____ **1) an article of clothing** (pants)
_____ **2) a type of fish** (shark)
_____ **3) a part of the body** (jaw)

Name/ID Number:_____ Number of words recalled:_____

Date:_____ Number of correct monitoring responses:_____

Number of words per list:_____

SEMANTIC WORD LIST

Form B

Instructions for Examiner: Give the subject the following instructions. Embellish as necessary to help them understand the task.

When administering the word list, present words at a rate of 1 per second. Present the target number quickly after the last word in the list; i.e. leave as small a pause as possible between the last word and the target number. This is done to prevent (or at least to minimize) maintenance rehearsal. If you notice a subject rehearsing the word list before beginning to count backwards, instruct them not to do so. Subjects are to count backward from the target number by increments of three for 9 seconds prior to being given the stimulus cue. If subjects do not respond encourage them once to guess, even if they claim to have no recollection. Be sure to record all responses. Even if the subjects correct themselves, be sure to write the first response as well as subsequent responses.

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Then I will give you some hints about the meaning of words on the list that I want you to remember.

For example, I might say "flannel, biscuit, tennis, 60." You would raise your finger as I say biscuit. Then you would start counting backward by two from 60 out loud (allow subject to start counting for a few seconds), then, if I said "a sport", you would say . . . (Allow subject to respond. If they say "tennis," say "good." If not, say that's not quite correct, tennis was the word on the list which was a sport.) Give next sample even if this one was done successfully.

Let's try another, "milk, hamster, spear, 90" (After a few seconds, say "a type of liquid.")

Let's do one more. "Gold, curb, sparrow, 90." A type of metal.

Now we are ready to start. Again, I will read you a list of words and you should listen for things that are edible. Then I will give you a number. Count backwards by two as soon as I give you the number. After you have been counting for a while, I will give you some hints about sounds of words on the list I want you to remember. Ready, let's begin.

Semantic Word List B
Page: 2

List 1

1) vest	1) vest	1) vest	1) vest	1) vest
2) toe	2) toe	2) blade	2) blade	2) blade
3) grape	3) blade	3) toe	3) toe	3) cloud
	4) grape	4) cloud	4) cloud	4) toe
		5) grape	5) lever	5) lever
			6) grape	6) mile
				7) grape

Starting number: 75

_____ **1) a part of the body** (toe)
_____ **2) an article of clothing** (vest)
_____ **3) a fruit** (grape)

List 2

1) cow	1) cow	1) cow	1) cow	1) cow
2) couch	2) sugar	2) sugar	2) sugar	2) sugar
3) pan	3) couch	3) couch	3) soup	3) soup
	4) pan	4) soup	4) couch	4) couch
		5) pan	5) army	5) army
			6) pan	6) thief
				7) pan

Starting number: 138

_____ **1) something from a kitchen** (pan)
_____ **2) a piece of furniture** (couch)
_____ **3) an animal** (cow)

List 3

1) belt	1) belt	1) belt	1) belt	1) belt
2) hand	2) bacon	2) bacon	2) bacon	2) bacon
3) gnat	3) hand	3) hand	3) straw	3) straw
	4) gnat	4) straw	4) hand	4) hand
		5) gnat	5) piano	5) piano
			6) gnat	6) rain
				7) gnat

Starting number: 89

_____ **1) something you wear** (belt)
_____ **2) an insect** (gnat)
_____ **3) a part of the body** (hand)

Semantic Word List B
Page: 3

List 4

1) pea	1) pea	1) pea	1) pea	1) pea
2) deer	2) deer	2) bread	2) bread	2) bread
3) hoe	3) bread	3) deer	3) deer	3) mast
	4) hoe	4) mast	4) mast	4) deer
		5) hoe	5) wall	5) wall
			6) hoe	6) tunnel
				7) hoe

Starting number: 171

_____ **1) a vegetable** (pea)
_____ **2) an animal** (deer)
_____ **3) a tool** (hoe)

List 5

1) spoon	1) spoon	1) spoon	1) spoon	1) spoon
2) bee	2) box	2) box	2) box	2) box
3) shoe	3) bee	3) bee	3) bath	3) bath
	4) shoe	4) bath	4) bee	4) bee
		5) shoe	5) rifle	5) rifle
			6) shoe	6) rose
				7) shoe

Starting number: 78

_____ **1) something you wear** (shoe)
_____ **2) something from the kitchen** (spoon)
_____ **3) an insect** (bee)

List 6

1) cat	1) cat	1) cat	1) cat	1) cat
2) peach	2) peach	2) paper	2) paper	2) paper
3) lung	3) paper	3) peach	3) peach	3) spear
	4) lung	4) spear	4) spear	4) peach
		5) lung	5) wax	5) wax
			6) lung	6) string
				7) lung

Starting number: 132

_____ **1) a fruit** (peach)
_____ **2) an animal** (cat)
_____ **3) an organ in the body** (lung)

Reid Skeel & Bruce Crosson, June 2, 1994

Semantic Word List B
Page: 4

List 7

1) bark	1) bark	1) bark	1) bark	1) bark
2) suit	2) suit	2) leg	2) leg	2) leg
3) stool	3) leg	3) suit	3) suit	3) dime
	4) stool	4) dime	4) dime	4) suit
		5) stool	5) paste	5) paste
			6) stool	6) net
				7) stool

Starting number: 67

_____ **1) something you wear** (suit)
_____ **2) a piece of furniture** (stool)
_____ **3) part of a tree** (bark)

List 8

1) goat	1) goat	1) goat	1) goat	1) goat
2) pot	2) candy	2) candy	2) candy	2) candy
3) ball	3) pot	3) pot	3) cigar	3) cigar
	4) ball	4) cigar	4) pot	4) pot
		5) ball	5) mat	5) mat
			6) ball	6) sack
				7) ball

Starting number: 164

_____ **1) an animal** (goat)
_____ **2) a toy** (ball)
_____ **3) something from the kitchen** (pot)

List 9

1) rake	1) rake	1) rake	1) rake	1) rake
2) corn	2) corn	2) trash	2) trash	2) trash
3) fly	3) trash	3) corn	3) corn	3) corn
	4) fly	4) land	4) land	4) land
		5) fly	5) ring	5) ring
			6) fly	6) hall
				7) fly

Starting number: 179

_____ **1) a tool** (rake)
_____ **2) a vegetable** (corn)
_____ **3) an insect** (fly)

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Semantic Word List B
Page: 5

List 10

1) hat	1) hat	1) hat	1) hat	1) hat
2) feet	2) tent	2) tent	2) tent	2) tent
3) dog	3) feet	3) feet	3) cave	3) cave
	4) dog	4) cave	4) feet	4) feet
		5) dog	5) tank	5) tank
			6) dog	6) wire
				7) dog

Starting number: 47

_____ **1) an animal** (dog)
_____ **2) something you wear** (hat)
_____ **3) a part of the body** (feet)

Name/ID Number_____

Date:_____

Number of Correct Responses for Each Type of Sentence

	Syntax/Noun	Syntax/Modifier	Semantic/Noun	Semantic/Modifier
Simple	#1	#2	#7	#8
Subordinate	#3	#4	#9	#10
Center-Embedded	#5	#6	#11	#12

Right	Wrong	
____	____	1) The van hit the blue truck. What was hit? **Truck**
____	____	8) The car hit the tall tree. What was tall? **Tree**
____	____	6) The boy that chased the girl was friendly. Who was friendly? **Boy**
____	____	11) The old, tired dog and the young, silly puppy chewed the fresh, tasty bone. What was chewed on? **Bone**
____	____	5) The cow that chased the donkey was angry. What chased? **Cow**
____	____	12) The tan, muscular gardener tended fragrant, red flowers and green, leafy bushes. What was tan? **Gardener**
____	____	2) The man tapped the short woman. Who was short? **Woman**
____	____	9) The furry, smart monkey held the rubber, striped ball. What was held? **Ball**
____	____	4) The bus hit the car that was speeding. What was speeding? **Car**
____	____	7) The cat slapped the purple yarn. What slapped? **Cat**
____	____	3) The skunk chased the porcupine that was hungry. What chased? **Skunk**
____	____	10) The smart, exact woman measured the warped, bent board. What was bent? **Board**

Right	Wrong	
____	____	3) The robin followed the oriole that was singing. What followed? **Robin**
____	____	12) The naive, young student and the elderly, experienced teacher studied a long, difficult equation. What was young? **Student**
____	____	2) The monkey followed the brown chimpanzee. What was brown? **Chimpanzee**
____	____	9) The big, gray elephant crushed the delicate, yellow flower. What did the crushing? **Elephant**
____	____	6) The dog that jumped the fence was big. What was big? **Dog**
____	____	11) The big, gray elephant and the swift, striped zebra crushed the delicate, yellow flower. What was crushed? **Flower**
____	____	1) The cat licked the brown dog. What was licked? **Dog**
____	____	8) The man stamped the gray letter. What was gray? **Letter**
____	____	5) The beaver that pursued the raccoon was tired. What pursued? **Beaver**
____	____	10) The meticulous, sweaty sailor washed the blue, wooden boat. What was blue? **Boat**
____	____	4) The airplane followed the helicopter that was new. What was new? **Helicopter**
____	____	7) The monkey held the yellow flower. What was held? **Flower**
____	____	1) The calf bit the tan cow. What was bitten? **Cow**
____	____	8) The woman felt the new sweater. What was new? **Sweater**
____	____	6) The bluebird that followed the canary was noisy. What was noisy? **Bluebird**

Right	Wrong	
____	____	11) The bald, sunburned man and the furry, rabid dog jumped the white, iron gate. What was jumped? **Gate**
____	____	5) The canoe that followed the rowboat was silver. What followed? **Canoe**
____	____	12) The pretty, feminine girl and the handsome, masculine boy went to the long, boring movie. What was handsome? **Boy**
____	____	2) The chicken pecked the noisy turkey. What was noisy? **Turkey**
____	____	9) The fierce, predatory wolf hunted the meek, scared mouse. What was hunted? **Mouse**
____	____	4) The boy hugged the girl who was friendly. Who was friendly? **Girl**
____	____	7) The farmhand milked the brown cow. What was milked? **Cow**
____	____	3) The monkey chased the chimpanzee that was happy. What chased? **Monkey**
____	____	10) The lazy, careless business man sent the overdue, expensive bill. What was overdue? **Bill**
____	____	3) The van hit the truck that was blue. What did the hitting? **Van**
____	____	12) The quick, thrifty shopper priced crisp, cold lettuce and warm, soft bread. What was cold? **Lettuce**
____	____	2) The little girl hugged the boy. Who was little? **Girl**
____	____	9) The playful, silly cat popped the green, round balloon. What did the popping? **Cat**
____	____	6) The raccoon that the skunk chased was fast. What was fast? **Raccoon**
____	____	11) The friendly, strong lumberjack chopped the tall, straight oak and the small, twisted sapling. What chopped? **Lumberjack**
____	____	1) The furry cat nipped the kitten. What nipped? **Cat**

Right	Wrong	
____	____	8) The red truck plowed the snow. What was red? **Truck**
____	____	5) The truck that the bus hit was white. What was hit? **Bus**
____	____	10) The athletic, spotted dog jumped the tall, wooden fence. What was spotted? **Dog**
____	____	4) The crab pinched the lobster that was angry. What was angry? **Lobster**
____	____	7) The smart dolphin chased the ball. What was chased? **Ball**
____	____	1) The brown donkey kicked the mule. What kicked? **Donkey**
____	____	8) The strong man crushed the can. What was strong? **Man**
____	____	6) The trout that the minnow followed was shiny. What was shiny? **Trout**
____	____	11) The brave, strong hunter attacked the small, helpless squirrel and the smelly, striped skunk. What attacked? **Hunter**
____	____	5) The mule that the donkey kicked was small. What was kicked? **Mule**
____	____	12) The efficient, careful maid cleaned the sturdy, brown table and the delicate glass chandalier. What was delicate? **Chandalier**
____	____	2) The hungry tiger ate the lion. What was hungry? **Tiger**
____	____	9) The frantic, hungry dog ate the moist, delicious meal. What did the eating? **Dog**
____	____	4) The banker called the lawyer who was tall. Who was tall? **Lawyer**
____	____	7) The stubborn mule kicked the can. What kicked? **Mule**
____	____	3) The submarine attacked the destroyer that was grey. What attacked? **Submarine**
____	____	10) The hungry, brown monkey ate the salty, round peanut. What was hungry? **Monkey**

Right	Wrong	
____	____	3) The chipmunk tackled the squirrel that was brown. What tackled? **Chipmunk**
____	____	12) The sleek, fast greyhound and the fat, slow turtle followed the long, winding trail. What was winding? **Trail**
____	____	2) The fast helicopter followed the plane. What was fast? **Helicopter**
____	____	9) The shy, caring girl brushed the mangy, barking dog. What did the brushing? **Girl**
____	____	6) The chipmunk that chased the squirrel was small. What was small? **Chipmunk**
____	____	11) The arrogant, dedicated chef cooked hot spicy tamales and bland, tasteless pudding. What cooked? **Chef**
____	____	1) The eagle chased the fast hawk. What chased? **Eagle**
____	____	8) The young boy built a fire. What was young? **Boy**
____	____	5) The turkey that the chicken pecked was hungry. What was pecked? **Turkey**
____	____	10) The friendly, happy horse ate the powdery, dry oats. What was friendly? **Horse**
____	____	4) The man slapped the butcher who was fat. Who was fat? **Butcher**
____	____	7) The playful kitten chased the feather. What chased? **Kitten**

BIOGRAPHICAL SKETCH

Reid Skeel was born in Seattle, Washington, in 1967. After earning a B.S. from Northwestern University in 1989, He began graduate study in general psychology at Georgia College in 1990, in Milledgeville, Georgia. He began his graduate study at the University of Florida in 1992. Mr. Skeel then completed the current study as his dissertation research and earned his doctoral degree in 1998.

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

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This dissertation was submitted to the Graduate Faculty of the College of Health Professions and to the Graduate School and was accepted as partial fulfillment of the requirements for the degree of Doctor of Philosophy.

August 1998

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